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BEARING ON HEREDITY AND VARIATION

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THE CYTOLOGY OF SOME WESTERN SPECIES OF
TRIMEROTROPIS (ACRIDIDAE)

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Received June 4, 1948

THE genus *Trimerotropis* (Acrididae: Oedipodinae) has formed the subject of cytological investigation, particularly by CAROTHERS (1917) and KING (1923). The eastern species (*T. citrina* and *T. maritima*) show the uniformly acrocentric diploid chromosome complement of 23 in the male which is characteristic of all the other Oedipodinae except the closely related genus *Circotettix*. The western species studied by CAROTHERS (*T. suffusa* Scudder), (*T. fallax* Saussure) and by KING (*T. thalassica* Bruner, *T. caeruleipennis* Bruner and *T. cyaneipennis* Bruner), while retaining the typical chromosome number, show a shift of the centromere in some of the chromosomes the number of which varies from species to species and from individual to individual within the species. The variation within the species is due to the fact that the centromere shift is found frequently in a heterozygous condition. Species of the closely related genus *Circotettix* (CAROTHERS 1917, 1921 and HELWIG 1929) show the same kind of centromere shift. While here the diploid number has been reduced to 21 by the disappearance of two of the shorter chromosomes the shift cannot be explained by a translocation of these chromosomes, if for no other reason, because many more than two chromosomes show the change of centromere position. Apparently a somewhat similar shift is found in the Cyrtacanthacrid genus *Indopodisma* (HELWIG 1942) which also shows a reduction to 21 chromosomes in the male.

The shift of centromere position must not be confused with the condition which is evolving in *Hesperotettix* and *Mermiria* (McCLUNG 1917) and which has become fixed in *Chorthippus*, *Chloealtis*, and others where the occurrence of metacentric chromosomes is associated with a corresponding reduction in the diploid complement. In such cases it seems clear that the metacentric chromosomes must have arisen through translocations. In *Trimerotropis*, *Circotettix* and *Indopodisma*, the shift in centromere position is related neither to reduction in numbers nor to increase in length of chromosomes. There must have been either a movement of the centromere from a point near the end (acrocentric) to a point much nearer the centre (metacentric) or the loss of a subterminal centromere and the formation of a new submedian one. This latter alternative runs counter to the almost universally accepted view of the constancy of the centromere as an essential chromosome organelle and I would not suggest it were it not for recent observations of RHOADES & VILKOMERSON (1942), PRAKKEN and MÜNTZING (1942), and ÖSTERGREN and PRAKKEN (1946) who have shown that in the case of certain strains of maize and rye another point in the chromosome can function exactly as the centromere in anaphase movement.

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If we, for the moment, exclude this rather remote possibility two alternative chromosome changes may be called upon to account for the centromere shift. The one that occurs most naturally to the mind is a pericentric inversion asymmetric with reference to the centromere. It is presumed that the original acrocentric chromosomes were not strictly telomitic. I have already shown (COLEMAN 1943) that in the case of some supposedly telomitic chromosomes, short arms exist and further observations have convinced me that this is a general feature of all supposedly telomitic chromosomes. In that case, a pericentric inversion would involve two breaks and reunions. This explanation for the shift obtains a certain amount of support from the fact that a pericentric inversion has been observed and documented by me in an individual of *Chorthippus longicornis* (COLEMAN 1947). In this case, however, the inversion has led to a shift of the centromere from a metacentric to an acrocentric position, the opposite to that which has happened in *Trimerotropis*.

In the case of *Chorthippus*, crossing over in the inversion has resulted in the production of chromosome duplications and deficiencies so generally as greatly to reduce sperm viability. One would expect a similar loss of fertility in *Trimerotropis* in cases where chromosome homologues are heterozygous for the inversion but, as a matter of fact, there is no evidence of this. MULLER (1940) accounts for this anomaly on the supposition that crossing over is prevented from occurring in the inverted region. It is true most of the figures published by CAROTHERS and KING indicate that chiasma formation has taken place toward the end farthest removed from the region of centromere shift. However, CAROTHERS (1921) figures terminal chiasmata at Metaphase I at the end where such an inversion must have taken place. These configurations show the homozygous condition but it is hard to see why heterozygosity for an inversion should lead to a complete blocking of chiasma formation.

HELWIG (1933) in his X-ray studies on *Circotettix*, although at first inclined to accept the theory of a pericentric inversion, later abandoned it on the ground that in his X-ray studies he found, among the abnormalities produced, no case of inversion.

None of the authors so far cited has dealt with any meiotic stage prior to first meiotic metaphase. However, WENRICH (1917) has described and illustrated pachyphase and diplophase configurations from a *Trimerotropis suffusa* male on the basis of smears provided by CAROTHERS. In this individual there were, according to WENRICH's illustrations, four bivalents showing the centromere shift in a homozygous, and two bivalents showing it in a heterozygous condition. His figure 8 on Plate 2, which purports to show various stages up to first meiotic metaphase in a heterozygous bivalent, appears to indicate failure of pachyphase pairing at both ends, but there is no indication of an inversion loop and it is to be doubted if the slight lack of pairing shown could be ascribed to what would have to be a fairly long inverted segment. If we judge from the metaphase configurations, it would have to involve more than one third the length of the metacentric univalent. Failure of pairing embraces a much shorter region than this. There seems to be no support in WENRICH's figures for the supposition that a pericentric inversion is responsible for the centromere shift.

As will be shown later, more extensive observations made by me point in the same direction.

WHITE, in his recently published *Animal Cytology* (1946) draws attention to the fact that, whereas the more easterly species of *Trimerotropis*, *T. maritima* and *T. citrina*, show no centromere shift, the western forms reported upon cytologically by CAROTHERS and KING all show this phenomenon, partly, at least, in a heterozygous condition. He advances the interesting suggestion that the striking difference in this connection may be related in some way to geographical distribution. Perhaps some slight support for this suggestion is furnished by the observations of HELWIG (1929) on chromosomal variations correlated with geographical distribution in *Circoletlix verruculatus*. HELWIG studied material collected from Massachusetts in the east and as far west as Michigan and found the Michigan forms with a greater proportion of atelomitic (metacentric) diads (univalents) in tetrads 1 and 8 than any of the more easterly forms. This would suggest that the more westerly forms are in a more labile condition cytologically.

The chance of collecting and studying western forms of *Trimerotropis* during the summer of 1947 made me decide to investigate firstly, whether chromosome changes in this genus are associated with geographical distribution as has been suggested by WHITE and secondly, whether early stages of meiosis in species showing heterozygosity for a centromere shift give any evidence of inversion loops as had been so clearly apparent in the case of the *Chorthippus* individual previously studied by me.

For slide preparation I used the method which has become standard in this laboratory and which gives better preparations than any others of the many tried. Testes are dissected out or squeezed out of decapitated males into Ringer's solution or directly into a fixing agent. LEVITSKY's chrome-formol consisting of equal parts of 1% chromic acid and 10% formalin was used in this case. The testes after washing are hydrolysed in normal HCl at 60°C for from 10-15 minutes and Feulgen stained. After washing in SO₂ water one to four testicular tubules are distributed on a slide in 50% acetic acid and covered with a cover glass. If the hydrolysis has been sufficient, slight tapping separates all the spermatocytes and distributes them evenly. Flattening with the use of filter or blotting paper and using quite heavy pressure separates the individual elements and brings them effectively into one plane. Microscopic examination is then carried out in the acetic acid at once or the preparations are made permanent by immersing them in dioxane for a few hours when the coverslip can be lifted without disturbing the material which usually sticks entirely to the coverslip. Mounting in dioxane balsam, xylol balsam, or clarite then gives excellent permanent preparations.

Collections were made in four localities on Vancouver Island, in Okanagan Valley of British Columbia and in the neighborhood of Walla Walla, Washington State. I have to thank DR. A. C. McCLARTY, pathologist in charge, DOMINION LABORATORY OF PLANT PATHOLOGY, Summerland, B. C. and MR. M. C. LANE, Entomologist in charge of Wire Worm Investigations at College Park, Washington for the laboratory and other facilities so kindly afforded to me.

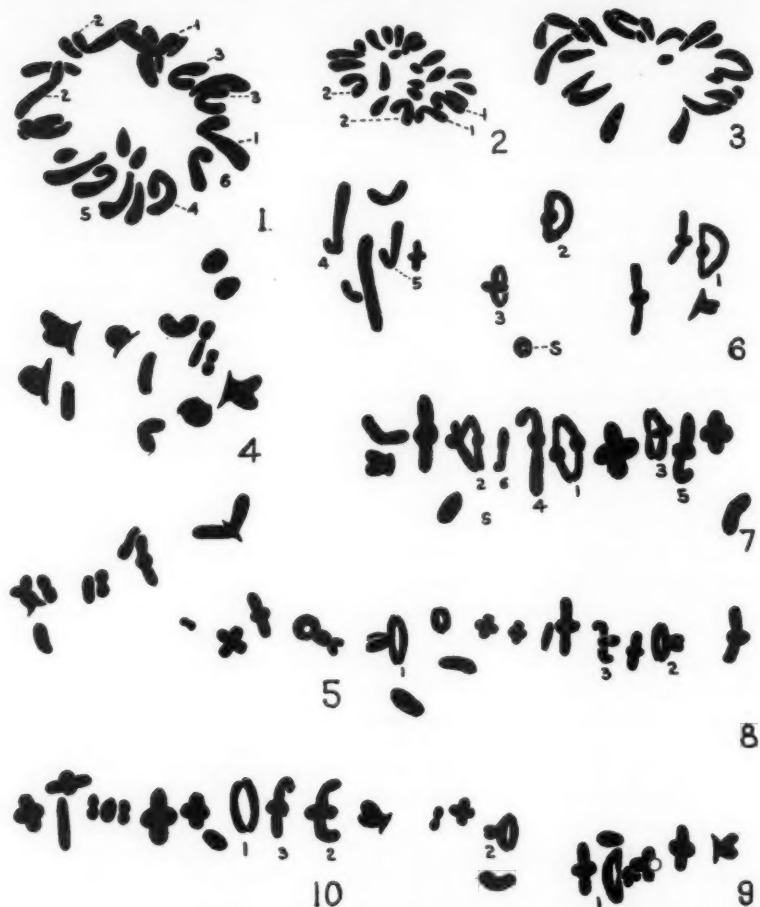


PLATE I

Explanation of Figures

FIGURE 1. Premeiotic metaphase of *Trimerotropis suffusa* showing three pairs of homozygous metacentric chromosomes labelled 1, 2, 3 and three single metacentrics labelled 4, 5, 6.

FIGURE 2. Premeiotic metaphase of *T. pallidipennis* showing two pairs of homozygous metacentric chromosomes.

FIGURE 3. Premeiotic metaphase of *T. praeclara* (?) showing exclusively acrocentric chromosomes.

FIGURE 4. First meiotic metaphase of *T. praeclara*.

FIGURE 5. First meiotic metaphase of *T. fontana*.

FIGURE 6. First meiotic metaphase of *T. suffusa* showing three homozygous metacentric bivalents, 1, 2, 3 and two heterozygous bivalents, 4, 5. The supernumary labelled S is probably an isochromosome.

FIGURE 7. First meiotic metaphase of *T. suffusa* showing three homozygous metacentric bi-

The material collected included the following species: *Trimerotropis suffusa*, *T. fontana* (*cerulaeipes*) and *T. pallidipennis* Burm. in different areas on Vancouver Island; *T. gracilis sordida* Walker at Summerland, Okanagan Valley, B. C.; *T. fontana* and a species tentatively identified by MR. LAWRENCE P. ROCKWOOD, Entomologist in charge U. S. BUREAU OF ENTOMOLOGY, Oregon, as *T. praeclara* McNeill, in the neighborhood of Walla Walla. There is, I think, no doubt of the identification of the first four species as they were checked by MR. E. R. BUCKELL, Entomologist DOMINION ENTOMOLOGICAL LABORATORY, Kamloops, B. C. an authority on British Columbia grasshoppers. The form given as *T. praeclara* was identified tentatively by MR. L. P. ROCKWOOD, Entomologist, U. S. BUREAU OF ENTOMOLOGY, Forest Grove, Oregon. Specimens sent for identification to DR. J. A. G. REHN did not arrive in sufficiently good condition to enable him to make any identification.

Of the five species studied, only one, *T. suffusa*, has been previously examined cytologically. My material, obtained from Mt. Douglas near Victoria, at Deep Cove, 20 miles north of Victoria on the Saanich peninsula and at Dashwood north of Nanaimo, resembled CAROTHERS' (1917) form B. of this species which was collected on Orcas Island, Puget Sound. While the form studied by this author showed homozygous metacentric bivalents varying from three to five in number, all of the individuals (about 20) examined by me showed no more than three such bivalents. There was also less variation in the number of heterozygous bivalents, the variation being from two to three as compared to two to six as reported by CAROTHERS. Plate I, figure 1 shows a premeiotic metaphase from a specimen collected at Deep Cove. The three pairs of homozygous metacentrics are marked 1, 2, 3; the three heterozygous metacentrics indicated as 4, 5, 6. Plate I, figure 7 from a specimen taken on Mt. Douglas shows three metacentric bivalents (1, 2, 3) and three tetrads (4, 5, 6) heterozygous for the centromere shift. This first meiotic metaphase plate also shows a supernumerary which from its position would seem to represent part of an X chromosome. Figure 6 shows a first metaphase plate from an individual captured at Deep Cove. In this is seen the same three metacentric bivalents as illustrated in figure 2. There are, however, here only two heterozygous bivalents. There is also a small supernumerary (S) which may possibly be a fragment homologous with the one found in the Mt. Douglas individual. However, its ring shape suggests that it may be an isochromosome. Similar fragments have been found by ROTHFELS (in the press) in his study of Neoploidism. He has been able to show with great probability that these super-

valents 1, 2, 3 corresponding to those in figure 6. There are three heterozygous bivalents, 4, 5, 6 of which the first two are homologous with those in figure 6.

FIGURE 8. First meiotic metaphase of *T. pallidipennis* showing three homozygous metacentric bivalents, 1, 2, 3.

FIGURE 9. First meiotic metaphase of another individual of *T. pallidipennis*. In this case there are only two homozygous metacentric bivalents, 1, 2.

FIGURE 10. First meiotic metaphase of *T. gracilis sordida* showing two homozygous metacentric bivalents 1, 2 and one heterozygous bivalent, 3. Magnification in all cases about 900 diameters.



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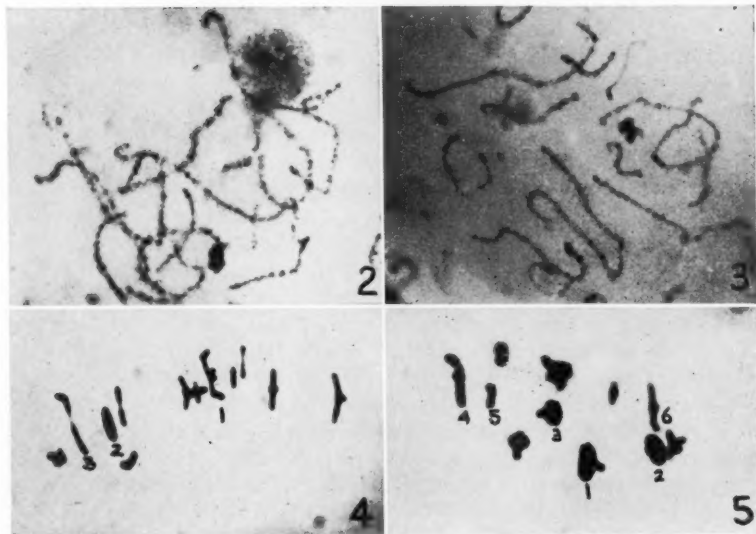


PLATE II

Explanation of Figures

FIGURE 1. Pachyphase chromosome complement of *T. gracilis sordida* showing almost perfect pairing which precludes the possibility of an inversion. One bivalent (above) has been broken by squashing.

FIGURE 2. Photomicrograph of pachyphase of *T. suffusa* showing apparently perfect pairing and absence of loc ps.

FIGURE 3. Photomicrograph of pachyphase of *T. gracilis sordida* showing apparently perfect pairing and absence of loop.

FIGURE 4. Photomicrograph of first meiotic metaphase of *T. gracilis sordida* showing two homozygous metacentric bivalents 1, 2 and one heterozygous bivalent, 3.

numerics have been derived partly from the X chromosome and partly by translocation from one of the smaller autosomes. Plate II, figure 5 reproduces a photomicrograph of a 1st metaphase plate of *T. suffusa* showing three homozygous and three heterozygous bivalents with the centromere shift. In addition to these observations on what appear to be centromere shifts that have become established in position, there is evidence of a much smaller shift with the centromere much closer to the end than in the cases illustrated. I propose examining more abundant material before reporting further on this.

Of the four other species examined, only two show any evidence of a centromere shift. These are *T. pallidipennis* and *T. gracilis sordida*. The other two, *T. fontana* and *T. praeclara*, show no evidence of it, the chromosomes being throughout acrocentric in all the individuals studied. It is thus clear that WHITE's tentative theory of the association of centromere shift with geographical distribution falls to the ground. *T. fontana* while not actually found associated with *T. suffusa* in the same localities has been found under very similar conditions. Thus *T. suffusa* was collected on Mt. Douglas near Victoria while *T. fontana* was found on Mt. Tolmie only about two miles distant from Mt. Douglas. It seems highly probable that the two species occur in both these areas as I made no very thorough search for them. To the person unfamiliar with the group the two species look much alike. Both have blue tibiae on the hind legs but *T. suffusa* is markedly larger. *T. praeclara* is a strikingly different species with orange red hind tibiae. As stated it also shows not the slightest evidence of centromere shift. Plate I, figure 3 shows a premeiotic metaphase of *T. praeclara*. Plate I, figure 4 shows a first meiotic metaphase of the same species. Plate I, figure 5 shows a first meiotic metaphase of *T. fontana* with no sign of centromere shift.

Both the remaining species show definite evidence of the centromere shift. *T. pallidipennis* was collected for me by MR. ROTHFELS along the east shore of Vancouver at a small beach north of Qualicum Bay. This material did not provide as satisfactory material for study as usual; so only 16 individuals could be analysed with certainty. A striking feature which is illustrated in Plate I figures 2, 8 and 9 was that the metacentric bivalents were throughout in a homozygous condition. At first, I was inclined to the view that, in this form, stability for the centromere shift must have been attained. However, while 14 out of 16 individuals showed three homozygous metacentric bivalents as illustrated in Plate I, figure 8, the other 2 showed only two such bivalents as shown in Plate I, figures 2 and 9. These two were a distinctly reddish colour variety of the species, but I think it highly improbable that this apparent correlation has any significance as there were intermediate color forms collected in the same area, and the area itself was so restricted as to make it highly improbable that varieties breeding true for such a cytological difference would be found.

The surprising thing is that no individuals were found showing heterozygosity for the centromere shift, for even if only one bivalent remains in a labile

FIGURE 5. Photomicrograph of first meiotic metaphase of *T. suffusa* showing three homozygous metacentric bivalents 1, 2, 3 and three heterozygous bivalents 4, 5, 6.

Figure 1 magnified about 1500 diameters; Figures 2-5 about 600 diameters.

condition one would expect a number of heterozygous individuals equal to those showing the two homozygous types. I hope to be able to continue the study of this species using a much larger number of individuals.

Turning to *T. gracilis sordida*, the last species examined by me, I was able to collect only three specimens, but they furnished me with, in many respects, the clearest and most easily analysed material studied. In all three specimens I found at first meiotic metaphase two bivalents homozygous and one bivalent heterozygous for a centromere shift. Plate I, figure 10 and Plate II, figure 2, reproduce typical first metaphase plates which show this clearly. The number of individuals was, of course, much too small to warrant even a guess as to the extent of homozygosity or heterozygosity in the species.

Preparations of *T. gracilis sordida* along with those of *T. suffusa* were most favorable for the study of zygo- and pachyphase stages for the possible occurrence of inversion loops. In most cases the heavy squashing necessary to spread out the chromonemata led to the disappearance of cell boundaries so that it was difficult to make out just where one spermatocyte ended and the other began. However, occasionally a spread could be obtained such as illustrated in Plate II, figure 1. Here the various bivalents can be identified, one marked by an arrow having been broken by the squashing. As will be seen, there is almost perfect pairing except at the extreme ends and there is not the slightest indication of an inversion loop. An examination of some hundreds of cells from both *T. gracilis sordida* and *T. suffusa* has shown no evidence whatever that an inversion loop is formed. Two photomicrographic reproductions of pachyphases are shown. Plate II, figure 2 is from an individual of *T. suffusa*, Plate II, figure 3 from an individual of *T. gracilis sordida*. Neither shows any sign of loops of any kind. It seems, therefore, that pericentric inversions must be ruled out as responsible for the centromere shift that has occurred in these species and we need not call upon MULLER's ingenious theory of inhibition of chiasma formation in an inverted segment.

How does it stand with a theory of lateral translocation? It would seem that here too there should be some evidence of failure of pairing. As is well known, it is very rarely that the centromere can be distinguished at this stage, but if any appreciable length of chromonema is contained in the translocated piece one would expect this to be revealed by lack of pairing with the non-translocated homologue in two regions, one near the end where the translocated piece has been removed and the other toward the middle where this piece has been inserted. The apparent failure of terminal pairing shown in WENRICH's Plate II, figure 8 (*loc. cit.*) might be interpreted as due to a transfer of a terminal or subterminal section containing the centromere, from one of the homologues through translocation, but there is no corresponding failure of pairing toward the middle of the bivalent as one should expect if a lateral translocation is responsible for the centromere shift. It seems certain that if a lateral translocation is responsible for the shift, the section involved can contain little if anything more than the centromere, for I have been able to find no evidence of even the slightest failure of pairing at pachyphase except at the ends of the homologous chromonemata.

There remains the possibility of a change in organisation involving the loss

of function of a centromere near the end of one of two homologues coinciding with the development of a new centromere from one of the chromomers in a metacentric position. It may be that HELWIG had something like this in his mind when he spoke of intrachromosomal reorganization producing a change of locus of fibre attachment. However, as he suggests that the change may have been a gradual process this seems rather unlikely.

As far as I am aware the only evidences for a *de novo* organization of a centromere at a new locus is that furnished by RHOADES and VILKOMERSON (1942) for a strain of maize and by PRAKKEN and MÜNTZING (1942) and ÖSTERGREN and PRAKKEN (1946) for a strain of rye. In both these cases (with special clearness in the case of maize) the authors have shown that, during first and second meiotic anaphase, movement appears to be controlled partially or almost entirely by terminal chromosome regions to which spindle fibres are attached just as they are to the normal centromere. However, in the case of both plants, this peculiar phenomenon is confined to the meiotic divisions and in neither case has the normal centromere disappeared or given up entirely its directive function. In Trimerotropis there is no evidence, as far as I have been able to observe up to the present, of any double centromere effect, but my preparations were not very suitable for such a study. The papers of CAROTHERS, KING, and HELWIG whose studies were based, in part at least, on sectioned material do not suggest the possibility of a double spindle fibre attachment of chromosomes but such an unexpected phenomenon might have been overlooked. An investigation of this possibility would be well worth while, more especially as there is evidence from other animal groups—Hemiptera (HUGHES SCHRADER and RIS 1941) and Scorpionidae (PIZA de TOLEDO 1941)—that the centromere is by no means universally a single localized chromosome organelle. Pending further evidence in this connection I should prefer to attribute the centromere shift to a lateral intrachromosomal translocation involving three breaks in the chromosome.

SUMMARY

1. Five western species of Trimerotropis, *T. suffusa*, *T. gracilis sordida*, *T. pallidipennis*, *T. fontana* and *T. praeclara*(?) have been examined cytologically, the last four for the first time.

2. Of the five, the first three show a centromere shift from an acrocentric to a metacentric position such as has been described for all the western species heretofore studied. Of these three the first two (*T. suffusa* and *T. gracilis sordida*) show both homo- and heterozygosity for the shift. The individuals of *T. pallidipennis* which were examined were collected in one small area and all showed a homozygous condition for the centromere shift.

3. The last two species, *T. fontana* and *T. praeclara* showed no centromere shift and were in this respect like the eastern species, *T. maritima* and *T. citrina*. The shift cannot, therefore, be correlated with geographical distribution as has been suggested by WHITE.

4. The centromere shift has not been due to a pericentric inversion as careful examination showed no trace of inversion loops, or of long unpaired segments at pachyphase such as would occur were such inversions present in the heter-

ozygous condition shown by some of the bivalents at metaphase.

5. If an intrachromosomal translocation is responsible for the shift it must have involved three simultaneous chromosome breaks. Further, the translocated segment must have comprised hardly anything more than the centromere, for in no case was there evidence of any submedian unpaired region at pachyphase. Anything more than a very minute segment would have led to a detectable unpaired segment. If one assumes that the terminal chromomere (telomere) can take part in an intrachromosomal translocation with the formation of a new telomere, there would, of course, be only two breaks involved in the centromere shift. However, the evidence for such a kind of change seems to me doubtful.

6. The possibility that the apparent shift is due to the disappearance of the original subterminal centromere and the organization of a new one in a submedian position, while it seems improbable, should not be entirely excluded.

LITERATURE CITED

- CAROTHERS, E. E., 1917 The segregation and recombination of homologous chromosomes as found in two genera of Acrididae (Orthoptera). *J. Morphol.* **28**: 445-494.
 1921 Genetical behavior of heteromorphic homologous chromosomes of *Circotettix* (Orthoptera). *J. Morphol.* **35**: 457-483.
- COLEMAN, L. C., 1943 Chromosome structure in the Acrididae with special reference to the X chromosome. *Genetics* **28**: 2-8.
 1947 Chromosome abnormalities in an individual of *Chorthippus longicornis* (Acrididae). *Genetics* **32**: 435-447.
- HELWIG, E. R., 1929 Chromosomal relations correlated with geographical distribution in *Circotettix verruculatus* (Orthoptera). *J. Morphol.* **47**: 1-27.
 1933 The effect of X-rays upon the chromosomes of *Circotettix verruculatus* (Orthoptera). *J. Morphol.* **69**: 265-312.
 1942 Unusual integrations of the chromatin in the Machaerocera and other genera of Acrididae (Orthoptera). *J. Morphol.* **71**: 1-26.
- HUGHES-SCHRADER, S. and RIS, H., 1941 The diffuse spindle attachment of coccids as verified by the mitotic behavior of induced chromosome fragments. *J. Exp. Zool.* **87**: 429-456.
- KING, R. L., 1923 Heteromorphic homologous chromosomes of three species of *Pseudotrimerotropis* (Orthoptera). *J. Morphol.* **47**: 1-27.
- MCCLUNG, C. E., 1917 The multiple chromosomes of *Hesperotettix* and *Mermiria*. *J. Morphol.* **29**: 519-605.
- MULLER, H. J., 1940 Bearings of the *Drosophila* work on systematics, *The New Systematics*, Ed. J. S. Huxley, Oxford University Press: 185-268.
- ÖSTERGREN, G. and PRAKKEN, R., 1946 Behaviour on the spindle of the actively mobile chromosome ends of rye. *Hereditas* **32**: 473-494.
- PIZA DE TOLEDO, S., 1941 Chromosomes with two spindle attachments. *J. Hered.* **32**: 423-426.
- PRAKKEN, R. and MÜNTZING, A., 1942 A meiotic peculiarity in rye simulating a terminal centromere. *Hereditas* **28**: 441-482.
- RHOADES, M. M. and VILKOMERSON, H., 1942 On the anaphase movements of chromosomes. *Proc. Nat. Acad. Sci.* **28**: 433-436.
- ROTHFELS, K., Complement, polyploidy, and supernumeraries in *Neopodismopsis* (Acrididae). *J. Morphol.* (in the press).
- WENRICH, D. H., 1917 Synopsis and chromosome organization in *Chorthippus* (*Stenobothrus*) *curtipennis* and *Trimerotropis suffusa* (Orthoptera). *J. Morphol.* **29**: 471-511.
- WHITE, M. J. D., 1945 *Animal Cytology and Evolution*, viii+375 pp. Cambridge: Cambridge University Press. 109-116.

GEOGRAPHIC VARIATION OF CHROMOSOME STRUCTURE IN *DROSOPHILA PROSALTANS*

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Drosophila prosaltans Duda, as other species of the same genus, shows intra-specific variation in the chromosome structure. These variations are caused, as in other species, mainly by inversions of chromosome segments which take place in the phylogeny. However, in *Drosophila prosaltans*, the hybrids between strains of geographically remote origin show also another type of aberration, which leads to failure of pairing of certain sections of the chromosomes in salivary gland cells, apparently unconnected with any rearrangement of the linear order of genes in the chromosomes involved. Furthermore, one of the strains has shown, as described by DOBZHANSKY and PAVAN (1943a), an arrangement of chromosome limbs not observed in other strains, this difference being due, presumably, to a translocation. Observations on these variations of chromosome structure are reported in the present article.

MATERIAL AND METHODS

The known geographic distribution of *D. prosaltans* extends from northern Mexico, through Central America, to southern Brazil and Paraguay (PATTERSON 1943, listed as *D. sellata*; DOBZHANSKY and PAVAN 1943b). Strains coming from the following localities have been used: Huichihuayan, state of San Luis Potosi, Mexico; Chilpancingo and Zopilote Canyon, state of Guerrero, Mexico; Guatemala City, Guatemala; Belem, state of Pará, Brazil; Bertioga and Iporanga, state of São Paulo, Brazil, and Rio de Janeiro, Federal District, Brazil (see map in DOBZHANSKY and STREISINGER 1944). The Mexican strains have been obtained through the courtesy of PROFESSOR J. T. PATTERSON of the UNIVERSITY OF TEXAS, the Guatemalan and Brazilian ones through that of PROFESSOR THEODOSIUS DOBZHANSKY, except for the Rio strain which had been collected by PROFESSOR H. SOUZA LOPES. The Belem strain served as the standard. Flies from all other strains were outcrossed to this standard, and the offspring were allowed to develop at room temperature and with optimal food conditions. Temporary acetic-orcein mounts were made of salivary glands and the chromosomes examined while the mount was still fresh. All possible crosses between the available strains were made, and chromosomes of all pure strains were also studied.

THE KARYOTYPE OF THE SPECIES

Metaphase chromosome groups seen in the giant neuroblasts of larval ganglia contain, in either sex, six chromosomes: two pairs are V-shaped and

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one pair rod-like (Plate I). In all the strains except Bertioga, the X and Y chromosomes form one of the V-shaped pairs, the other V and the rod being autosomes (the second and third chromosomes).

In the salivary gland cells, five euchromatic strands can be seen radiating from a chromocenter. No dot-like bodies are present (cf. WHARTON 1943).

The correspondence between the designations of chromosome limbs given in Plate I and those given by DOBZHANSKY and PAVAN (1943a) is as follows (the designations of these authors are given to the right):

- X L corresponding to the X 1 strand
- X R corresponding to the X 2 strand
- II L corresponding to the A strand
- II R corresponding to the B strand
- III corresponding to the C strand.

When the chromocenter in a salivary gland cell is crushed by pressure of a cover slip, the two limbs of the second chromosome (II L and II R) are seen to include almost the entire mass of the chromocenter. The two limbs of the X are connected by a small amount of diffuse heterochromatin, and the base of chromosome III has also a small heterochromatic section. This structure resembles the condition described in *D. nebulosa* by PAVAN (1946b). In the salivary gland cells, the heterochromatin of the second chromosome is much more voluminous than that of the X, although at metaphase the two chromosomes seem to be about equally large. The Bertioga strain is aberrant, since one of the V-shaped chromosomes consists of an autosomal (III) and a heterochromosomal part (X R), while the other part of the X is free and appears as a rod-like chromosome (X L). Whether this peculiar structure is a racial trait of the Bertioga population, or a property of only a single strain, remains to be determined.

In Plate I, the chromosomes are subdivided, for descriptive purposes, into one hundred sections. The X L-chromosome contains sections 1 to 17, X R—18 to 35, II L—36 to 55, II R—56 to 75, and III—76 to 100.

DESCRIPTION OF THE CHROMOSOMES

X-chromosome—The X-chromosome can be identified by its paler and somewhat thinner appearance in male than in female larvae, and has a small amount of heterochromatin connecting the two limbs. The X L limb is the shortest of the five strands composing the chromosome set. It has its free end expanded to various extents in different cells. When the degree of expansion is considerable, the discs become partly invisible, and the end of the chromosome appears to be heterochromatic. Two rather short regions in the distal portion and two in the proximal portion of X L look, in some cells at least, like typical heterochromatin. There are five "weak places" (shown in Plate I by arrows) where the chromosome is very frequently ruptured by pressure of the cover slip. The gene arrangement in the X L is uniform in all the strains examined. The limb designated X R has a bulb-like swelling on the subterminal portion (section 34), while the free end is expanded into a fan-like structure (section 35). In

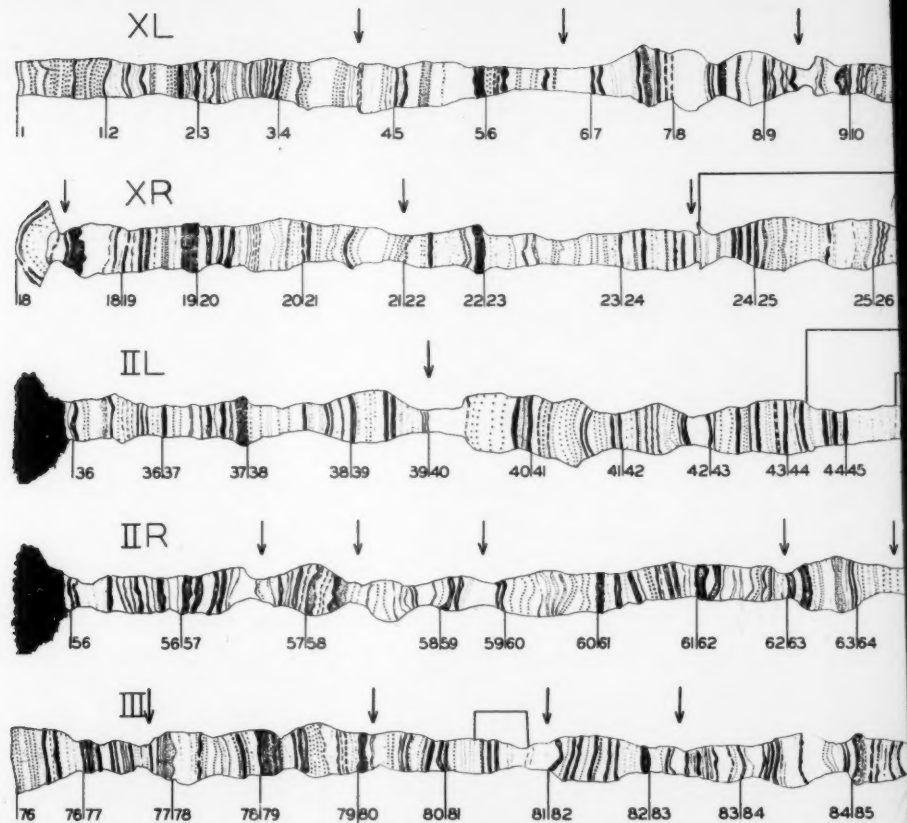
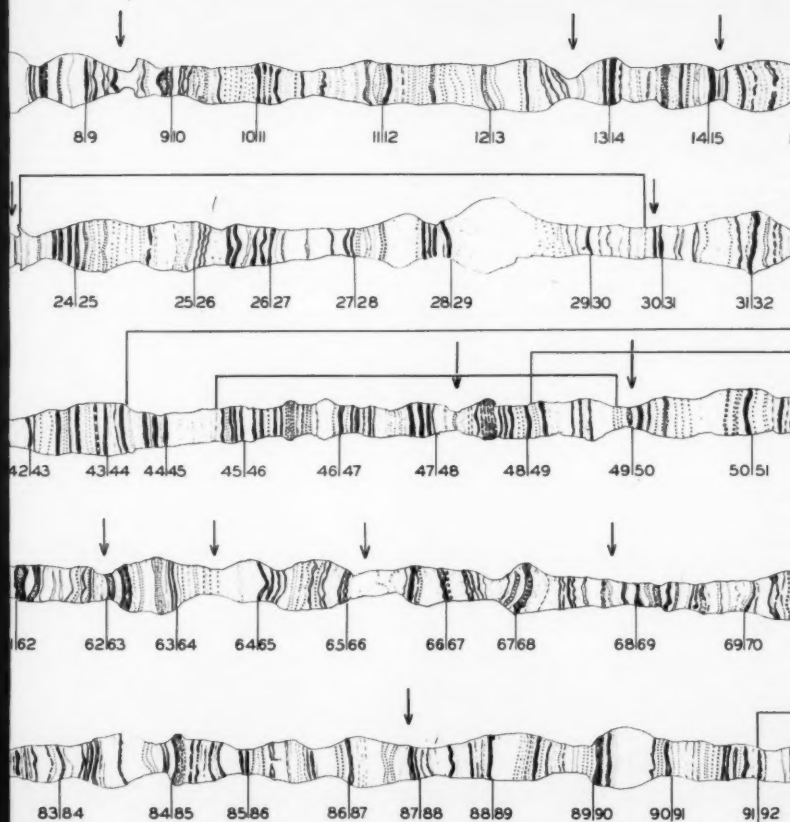
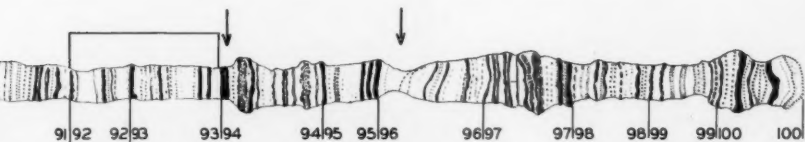
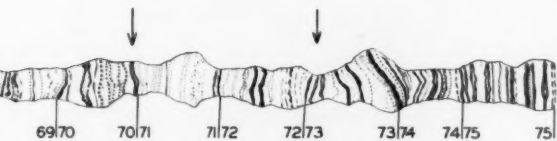
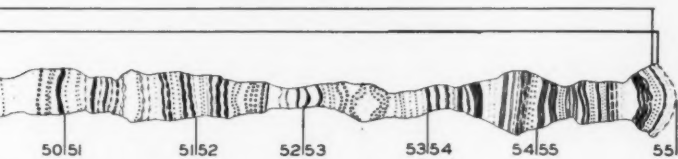
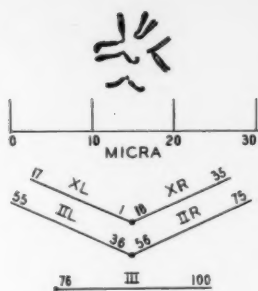
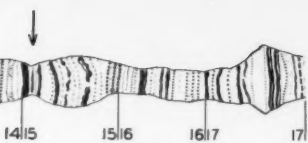


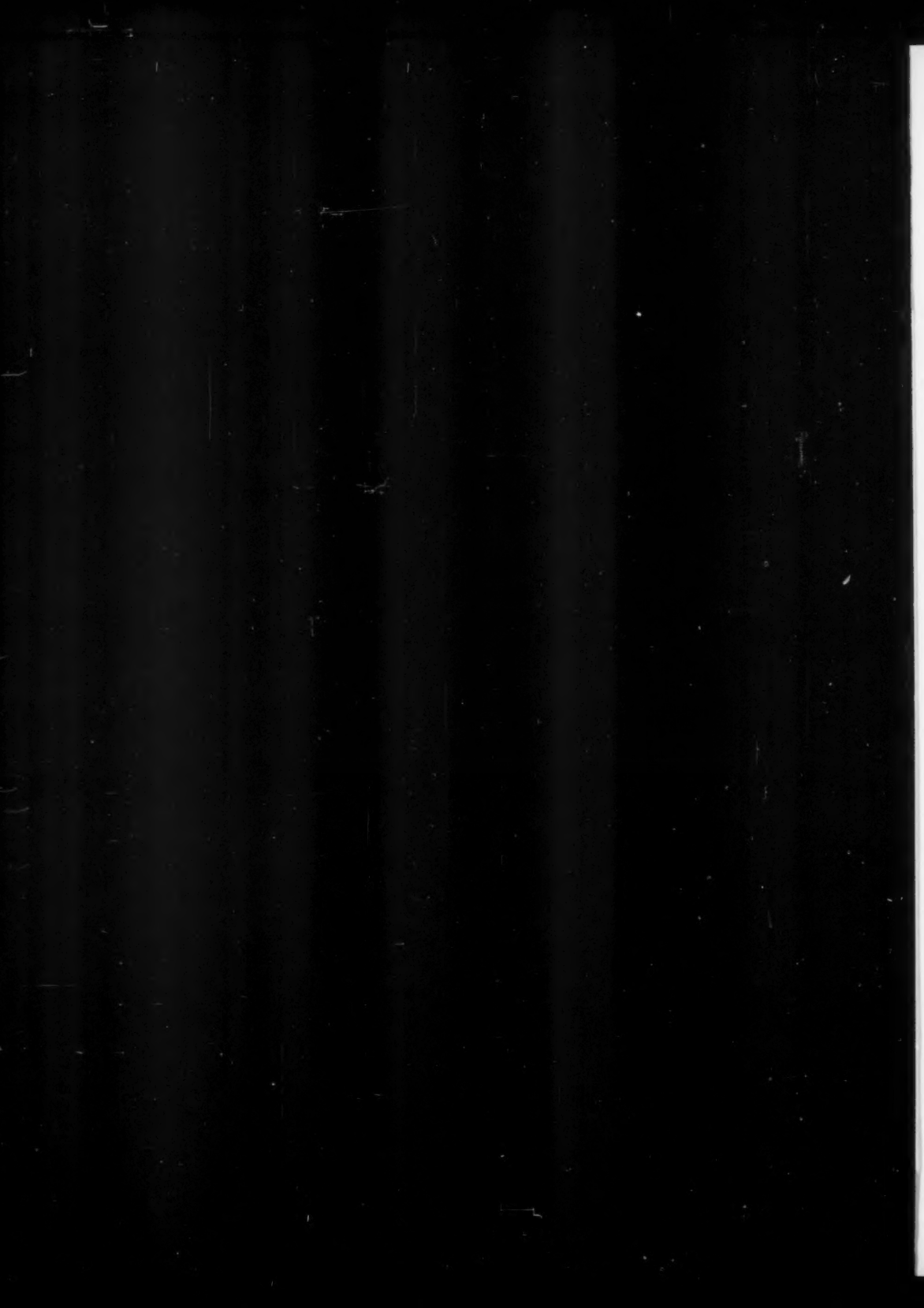
PLATE I. Composite map of the salivary gland chromosomes of *Drosophila melanogaster* showing "breakage places" where the chromosomes are frequently broken in preparations. Up



gland chromosomes of *Drosophila prosaltans* Duda. Sections involved in various inversions are repeatedly broken in preparations. Upper right: a metaphase chromosome group drawn on the same scale as the



Regions are represented by full lines; arrows indicate "weak" regions. Scale as the maps.



some cells, the fan-like structure appears heterochromatic. Proximally from the subterminal bulb there is an apparently heterochromatic region, in which the chromosome is frequently broken. This "weak point" is followed, proximally, by a region that appears frequently as two bulbs (sections 28 and 29), but in some cells the bulbous inflations are not formed. Three other places at which the chromosome is often fractured are shown by arrows in Plate I.

Second chromosome—As stated above, the chromocentral portion of the second chromosome contains a large mass of heterochromatin. The situation observed in *D. prosaltans* is, in this respect, exactly like that described by PAVAN (1946a) in *D. nebulosa*. The left limb of this chromosome (II L) can easily be identified by its characteristic base and tip as well as its general euchromatic character. The section 40 contains a very weak place at which the chromosome is very often broken. On the other hand, the right limb (II R) contains numerous heterochromatic regions and only very rarely can be seen fully stretched. Considerable difficulties have been found in preparing the drawings of the disc patterns in this chromosome, since it is very frequently broken into sections or shows heterochromatic intercalary associations which can be easily mistaken for inversions. The two inversions shown in this chromosome in figure 2B of the paper of DOBZHANSKY and PAVAN (1943a) have not been seen in our slides, and very likely represent such simulation of inversions by heterochromatic pairing. The boundaries of the heterochromatic and euchromatic sections vary from cell to cell, in a manner resembling that found in *D. pallidipennis* (DOBZHANSKY 1944).

Third chromosome—This chromosome has two large bulbous swellings (sections 78 and 90) which serve as good identification landmarks. Furthermore, this chromosome contributes little heterochromatin to the chromocenter, and is accordingly often seen separated from the latter.

VARIATION OF THE GENE ARRANGEMENT

X-chromosome—In the strains examined, no variations in the gene arrangement were found in the X L. The standard gene arrangement in the right limb (X R) occurs in all the strains except in those of Iporanga and Bertioga. In hybrids between Iporanga or Bertioga and any other strains, there is found a moderately large submedian inversion which includes sections 25 to 30 (figure 3C). The ends of this inversion coincide with two "weak points" at which the normal chromosome is often broken. The inverted gene arrangement seems to be confined to strains from southern Brazil.

Second chromosome—No variations in the gene arrangement in the right limb (II R) have been found among the strains examined. Conversely, the left limb of this same chromosome (II L) is most variable. Four different gene arrangements have been detected in II L. The standard gene arrangement will be designated as the A-arrangement, and the other three as the B, C, and D arrangements. Arrangement B differs from A by a long inversion extending from approximately the middle of section 44 of the standard map to the distal third of section 55, not far from the free end of the chromosome (figure 1 Belem-Iporanga). The inversion which transformed A into B is sufficiently

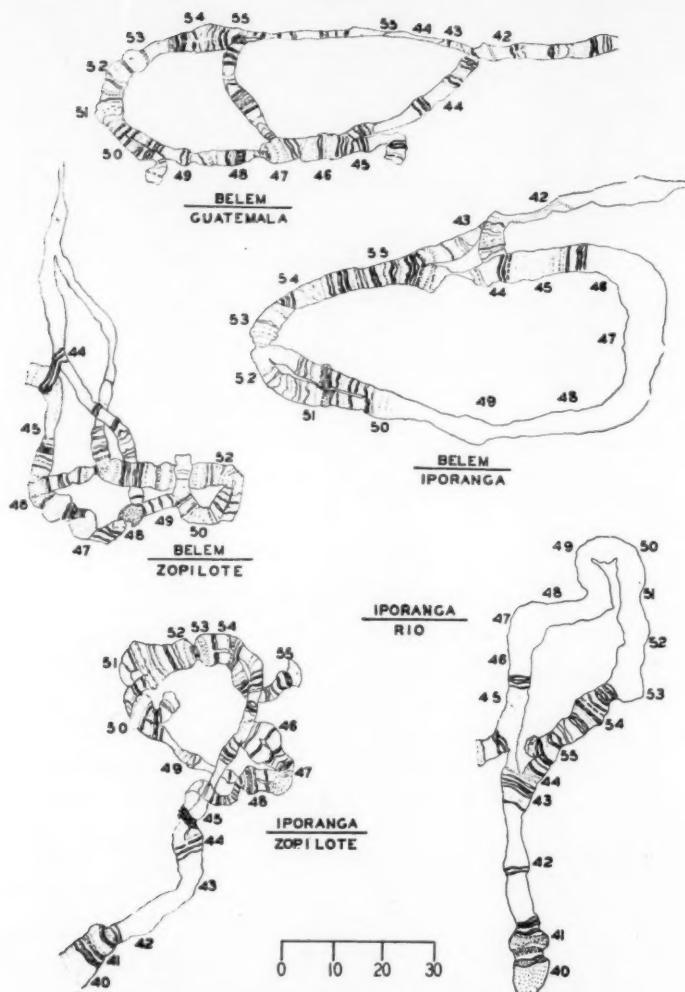


FIGURE 1. Inversions in the II L chromosome of *D. prosallans*.
 Belem-Guatemala—heterozygote for gene arrangements B-C.
 Belem-Iporanga—heterozygote for gene arrangements B-A.
 Belem-Zopilote—heterozygote for gene arrangements B-D.
 Iporanga-Rio—heterozygote for gene arrangements A-B.
 Iporanga-Zopilote—heterozygote for gene arrangements A-D.

close to being terminal so that the appearance of the free end of II L in B homozygotes is quite different from that in A homozygotes (compare figure 2 above and Plate I). Arrangement C is derived from A by a single inversion. This inversion begins at the boundary of sections 48 and 49, and extends up to and includes section 55, except for the terminal disc of the standard map (figure 1, Belem-Guatemala). This inversion is, accordingly, even more nearly terminal than that which gave rise to the B arrangement. The two inversions are broadly overlapping; the distal break in C is closer to the free end than that in B; the proximal breaks are rather far apart. In C homozygotes the distal end of the chromosome differs greatly both from A and B homozygotes (compare figure 2 below and Plate I). Heterozygotes which carry one A and one C chromosome exhibit, as expected, a double inversion configuration (figure 1,

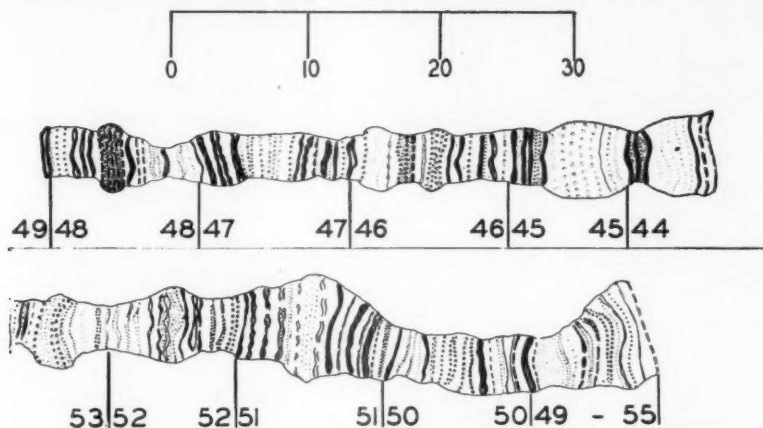


FIGURE 2. Free ends of chromosome II L in homozygotes for the gene arrangements B (top) and for C and D (below).

Belem-Guatemala). Arrangement D is derived from C by a single inversion. This inversion includes sections 45, 46, 47, 48, the first dark disc of 49, and 55. It can be seen that the inversion which transformed C into D overlaps that by which C arose from A. The overlapping part includes section 55. Heterozygotes carrying chromosomes A and D have a double inversion (figure 1, Iporanga-Zopilote). The combination B/D has the most complex configuration which involves a triple inversion (figure 1, Belem-Zopilote).

From the above data, on the basis of the theory of overlapping inversions, the following relationships of the four gene arrangements in the second chromosome can be deduced:

$$B \leftrightarrow A \leftrightarrow C \leftrightarrow D$$

Third chromosome—Two gene arrangements are recorded in this chromosome. One of them, the standard, occurs in all Brazilian strains, and the other is found in all Mexican and Guatemalan strains. The hybrids between these two groups of strains show two independent inversions in the third chromo-

some. The proximal inversion (fig. 3B) is rather short, and includes only a part of section 81. The distal inversion is longer, and extends from section 92 to 93 inclusive (fig. 3A). No chromosomes have been found with only the proximal or distal inversions.

FAILURES OF PAIRING IN THE THIRD CHROMOSOME

In the hybrids between strains of Brazilian and Mexican (or Guatemalan) origin, the third chromosome shows in addition to the inversions described

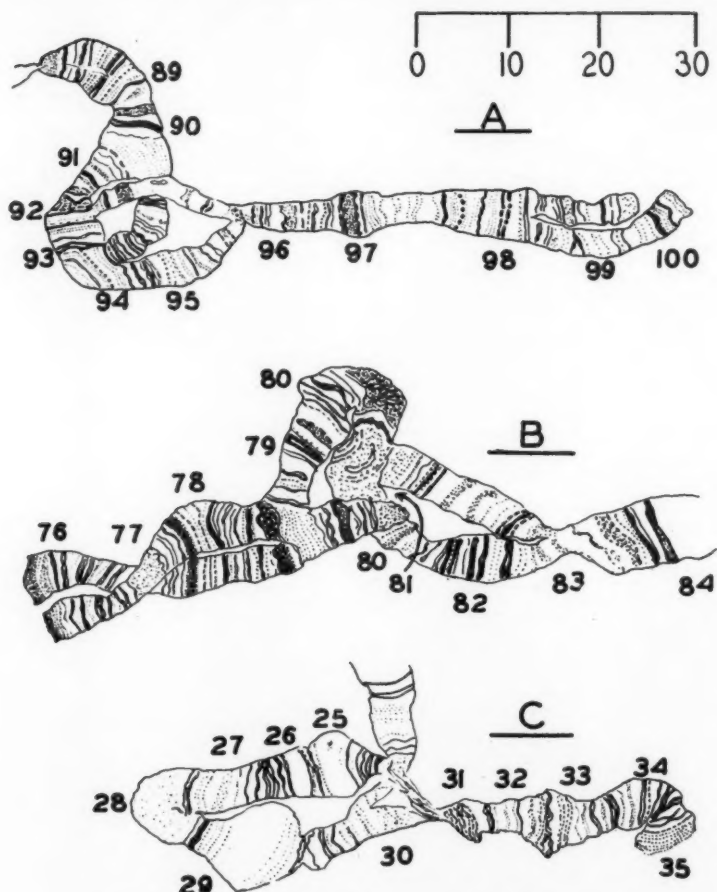


FIGURE 3. Inversions in the third chromosome and X R chromosome.
 A—distal inversion in the third chromosome.
 B—proximal inversion in the third chromosome.
 C—inversion in the X R chromosome.
 A and B exhibit characteristic failure of pairing at the distal and proximal extremities respectively (see text).

above, a failure of pairing of the proximal and of the distal portions. This failure of pairing is so constant and characteristic that it can be used as a criterion for recognition of the hybrid nature of a given larva (fig. 3A, B). The extent of the unpaired regions is, however, somewhat variable. In some cells, the distal unpaired region includes sections 98 to 100, in others only 99 to 100, or section 100 alone, or a part of it is unpaired, forming a Y-shaped figure. The subbasal unpaired region usually includes sections 76 to 78 (fig. 3B). In the distal unpaired region, one of the chromosome homologues appears usually shorter and more compressed than the other. This observation led at first to the supposition that the shorter strand was deficient in some sections or discs. But a more careful analysis has shown that, in favorable cells with well stretched chromosomes, the disc patterns in the unpaired homologues are quite alike. No difference in length is observed in the proximal unpaired region, but here one can frequently see a pairing of a few discs in section 77 followed and preceded by parts in which no pairing occurs. The disc patterns in the unpaired sections of the homologous chromosomes correspond. No regular failures of pairing occur either in hybrids between different Brazilian strains, or in those between different Mexican and Guatemalan strains.

Failures of pairing between apparently homologous sections of chromosomes in salivary gland cells have not been recorded in hybrids of strains of the same species. Such failures of pairing occur, however, not infrequently in hybrids between species. They were described first in the hybrids between *Drosophila melanogaster* and *D. simulans* (PÄTAU 1935) and in the hybrids of *D. pseudoobscura* and *D. persimilis* with *D. miranda* (DOBZHANSKY and TAN 1936). PATTERSON, STONE and GRIFFEN (1940) found a similar lack of pairing in hybrids of species belonging to the *virilis* group. Failures of pairing in interspecific hybrids were described also in the *guarani* group of the genus *Drosophila* by KING (1947).

GEOGRAPHIC DISTRIBUTION OF THE GENE ARRANGEMENTS

Whenever variation was found in the gene arrangement in any one chromosome, each variant gene arrangement occurred in strains from a certain geographic region. Thus, the standard arrangement in X R is the only one existing in strains from Mexico, Guatemala, and from Belem and Rio in Brazil. The strains from southern Brazil (Iporanga and Bertioga) are homozygous for the gene arrangement which differs from the standard by a single inversion (see above). Among the gene arrangements in the second chromosome, arrangement A is found in Bertioga and Iporanga strains which are homozygous for A, and in Belem which contains also arrangement B. Arrangement B is homozygous in the Rio strain and is carried in that from Belem. The strain from Guatemala is homozygous for arrangement C, which occurs also in the Huichihuayan strain together with D. Finally, the Chilpancingo and Zopilote strains are homozygous for D.

The phylogenetically related A and B arrangements occur, consequently, in Brazil, while the related C and D are found in Guatemala and Mexico. In only two strains, those from Belem and from Huichihuayan, two different gene arrangements are found. As shown above, one of the two known gene arrange-

ments in the third chromosome occurs in South America, and the other in Central America.

SUMMARY

In natural populations of *Drosophila prosaltans*, variations in the gene order caused by inversions are recorded in some of the chromosomes. The numbers of different gene arrangements found in each chromosome are as follows:

Left limb of X-chromosome.....	1 gene arrangement
Right limb of X-chromosome.....	2 gene arrangements
Left limb of second chromosome.....	4 gene arrangements
Right limb of second chromosome.....	1 gene arrangement
Third chromosome.....	2 gene arrangements

One of the strains differs from all others by a translocation between the X and the third chromosome. Finally, hybrids of Brazilian and Central American strains invariably show characteristic unpaired regions in the basal and terminal portions of the third chromosome. These failures of pairing are not due to any appreciable difference of the gene arrangements in the unpaired sections. Each chromosomal type is restricted to a definite portion of the geographic distribution area of the species.

ACKNOWLEDGEMENTS

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LITERATURE CITED

- DOBZHANSKY, TH., 1944 Distribution of heterochromatin in the chromosomes of *Drosophila pallidipennis*. Amer. Nat. **78**: 193-213.
- DOBZHANSKY, TH., and C. PAVAN, 1943a Chromosome complements of some south-Brazilian species of *Drosophila*. Proc. nat. Acad. Sci. **29**: 368-375.
- 1943b Studies on Brazilian species of *Drosophila*. Boletim Fac. Fil. Ciencias e Letras. Univ. São Paulo n. 36—Biologia Geral n 4. S. Paulo.
- DOBZHANSKY, TH., and G. STREISINGER, 1944 Experiments on sexual isolation in *Drosophila*. II Geographic strains of *Drosophila prosaltans*. Proc. nat. Acad. Sci. **30**: 340-345.
- DOBZHANSKY, TH., and C. C. TAN, 1936 Studies on Hybrid sterility. III. Z.I.A.V. **72**: 88-114.
- KING, J. C., 1947 A comparative analysis of the chromosomes of the *guarani* group of *Drosophila*. Evolution **1**: 48-62.
- PÄTAU, K., 1935 Chromosomenmorphologie bei *Drosophila melanogaster* und *Drosophila simulans* und ihre genetische Bedeutung. Naturw. **23**: 537-543.
- PATTERSON, J. T., 1943 I. The *Drosophilidae* of the Southwest. The Univ. of Texas Publ. 4313: 7-216.
- PATTERSON, J. T., W. STONE, and A. B. GRIFFEN, 1940 XI. Evolution of the *virilis* group in *Drosophila*. The Univ. of Texas Publ. 4032: 218-250.
- PAVAN, C., 1946a Chromosomal variation in *Drosophila nebulosa* Genetics **31**: 546-557.
- 1946b Two types of heterochromatin in *Drosophila nebulosa* Proc. nat. Acad. Sci. **32**: 137-145.
- WHARTON, L. T., 1943 Analysis of the metaphase and salivary chromosome morphology within the Genus *Drosophila*. The Univ. of Texas Publ. 4313: 282-319.

GENETICS OF NATURAL POPULATIONS. XVII. PROOF OF
OPERATION OF NATURAL SELECTION IN WILD POP-
ULATIONS OF *DROSOPHILA PSEUDOOBSCURA*

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INTRODUCTION

Most natural populations of *Drosophila pseudoobscura* are mixtures of individuals homozygous and heterozygous for gene arrangements in the third chromosome. The relative frequencies of the gene arrangements in populations show geographical and temporal variations. On Mount San Jacinto and in the Sierra Nevada in California, and in some localities in Texas, the temporal variations are cyclic and connected with the succession of the seasons (DOBZHANSKY 1943, 1948, DOBZHANSKY and EPLING 1944). It has been inferred that the seasonal changes in the frequencies of the gene arrangements are caused by natural selection. Carriers of different chromosomal types possess different adaptive values, and different types are favored at different seasons. This hypothesis has been indirectly confirmed by experiments on artificial populations which contained mixtures of different gene arrangements. Under certain conditions, changes in the relative frequencies of gene arrangements are observed from generation to generation in such artificial populations (WRIGHT and DOBZHANSKY 1946, and unpublished data). Analysis of these changes shows that, with rare exceptions, individuals of which the third chromosomes differ in gene arrangement (inversion heterozygotes) are superior in fitness to inversion homozygotes. An independent proof of the adaptive superiority of the heterozygotes to the homozygotes is as follows: Among the eggs deposited in the cages containing the artificial populations, inversion heterozygotes and homozygotes occur with relative frequencies approaching that demanded by the HARDY-WEINBERG rule. Yet, among the adult flies developed in the same population cages, excesses of heterozygotes and deficiencies of homozygotes are observed (DOBZHANSKY 1947a). It follows, then, that carriers of different gene arrangements interbreed at random in the population cages, and that a differential mortality between the egg and the adult stage upsets the HARDY-WEINBERG equilibrium proportions.

As a working hypothesis, it may be assumed that in natural populations likewise, the fitness of inversion heterozygotes is higher than that of homozygotes, and that the observed temporal changes in the natural populations are connected with this difference in fitness. If this hypothesis is valid, the homozygotes will be less and the heterozygotes will be more frequent among the flies found in nature than would be expected on the basis of the HARDY-WEINBERG equilibrium. The present article describes an attempt to test this working hypothesis.

* Observational data by TH. DOBZHANSKY, mathematical analysis by H. LEVENE.

METHOD

It should be noted that departures from the HARDY-WEINBERG equilibrium may result from causes other than selection, and that selection does not necessarily produce deviations from this equilibrium. Thus, excesses of homozygotes may be produced by inbreeding (e.g., mating of sibs shortly after emergence from pupae, or preferential mating of relatives), assortative mating, or random differentiation into sub-populations within the territory from which the samples are collected. The last contingency is excluded, because the mobility of adult *Drosophila pseudoobscura* is known to be considerable in relation to the size of collecting territories (DOBZHANSKY and WRIGHT 1943). Causes leading to deficiencies of homozygotes do not seem to be frequent in nature, though preferential mating of carriers of different genotypes might produce such deficiencies. All of the above causes of deviations from equilibrium proportions may be subsumed under the category of departures from panmixia; the deviations so produced will be discoverable at all stages of the life cycle.

Selection operating through differential mortality at any stage of the life cycle will cause departure from the HARDY-WEINBERG equilibrium at that stage and at all later stages, but not at earlier stages. On the other hand, selection operating through differential fecundity or sexual activity of adult flies would cause no disturbance of this equilibrium at any stage of the life cycle, provided that the population is panmictic. It follows that the effects of departures from panmixia and of differential mortality in the egg stage can be distinguished from those of differential mortality at any stage after egg hatching. For this purpose, samples of adult flies are collected in natural habitats and analyzed in two ways. First, females which had been fertilized before capture are permitted to lay eggs in individual cultures. The larvae are raised under optimal conditions at which little selection occurs (see WRIGHT and DOBZHANSKY 1946), and the chromosomes of one full grown larva from each culture are examined. These samples of larvae can be considered random samples of the eggs that would have been laid in nature by the females, and they can be used to test for panmixia. Such data will be called egg samples. Second, the males, caught in natural habitats at the same time, are individually mated to females of known chromosome constitution, and chromosomes of the resulting larvae are examined. Seven larvae (before 1945) and six larvae (during and since 1945) are examined. The first larva examined discloses one of the paternal chromosomes. The remaining larvae have a probability $63/64$ or $31/32$ of disclosing the other paternal chromosome. The wild adult males are thus classified as to karyotype, except that on the average $1/64$ or $1/32$ of the heterozygotes present are incorrectly classified as homozygotes. This type of data will be called adult male samples and can be used to test for selection, if egg samples have shown panmixia to hold. For more details about the methods used see DOBZHANSKY and EPLING (1944).

PANMIXIA IN NATURAL POPULATIONS

Extensive data on the incidence of homo- and heterozygotes in natural populations have been published by DOBZHANSKY and EPLING (1944). These

data were collected, whenever possible, by examining a single larva in the offspring of each wild female, and represent accordingly what has been called above "egg samples." However, some "adult male samples" have also been included. On the basis of such data DOBZHANSKY and EPLING concluded that panmixia obtained in natural populations of *Drosophila pseudoobscura*. This evidence needs reexamination for two reasons. First, many of the samples reported were combined egg and adult male samples, although egg samples decidedly predominated because they required much less labor in the laboratory. Second, χ^2 was calculated by an incorrect method. The correct method can be exemplified for a hypothetical sample having only ST and CH chromosomes. Let a , b , c be the number of ST/ST, ST/CH, CH/CH individuals (egg or adult males) observed. Then $p = (2a+b)/2(a+b+c)$ and $q = (2c+b)/2(a+b+c)$ are the proportions of ST and CH chromosomes observed. The "expected" numbers under the HARDY-WEINBERG equilibrium are then approximately $Ea = np^2$, $Eb = 2npq$, $Ec = nq^2$, where $n = a+b+c$. We then compute

$$\chi^2 = \frac{(a - Ea)^2}{Ea} + \frac{(b - Eb)^2}{Eb} + \frac{(c - Ec)^2}{Ec}.$$

Then, if the expected values are not too small, χ^2 will have the Chi-square distribution, but not—as might appear at first glance—with two degrees of freedom. The number of degrees of freedom is the number of entries that can be made arbitrarily without changing the expected values. Now in the present case, if a be specified, then we must have $2a+b=2np$, which fixes b for constant n and p , and when b is fixed the relation $2c+b=2np$ fixes c . Hence if we consider all tables with the same expected values, and hence with the same n , p , q , we find that only one entry is arbitrary, and we have only one degree of freedom for χ^2 . Now the method used by DOBZHANSKY and EPLING was to calculate

$$Y^2 = \frac{[(a+c) - (Ea+Ec)]^2}{Ea+Ec} + \frac{(b-Eb)^2}{Eb},$$

i.e. a " χ^2 " based on only two classes, homozygotes and heterozygotes. It is easy to show that Y^2 is always less than or equal to our previous χ^2 when computed from the same sample. Hence if χ^2 is distributed as Chi-square with one degree of freedom, Y^2 cannot be so distributed, and the use of the Chi-square table with Y^2 leads to P values which are too high. In general, if there are r different gene arrangements in a sample, there will be $r(r+1)/2$ possible genotypes, and χ^2 when computed in the obvious manner will have $[r(r+1)/2] - r$, or $r(r-1)/2$ degrees of freedom. Again, in this general case, a " χ^2 " based only on number of homozygotes and number of heterozygotes will not have a Chi-square distribution. The general χ^2 with $r(r-1)/2$ degrees of freedom is unsatisfactory, first because the expected numbers of some rarer genotypes are usually so small as to make the Chi-square table inapplicable, and second because significant values of χ^2 can be caused by discrepancies of many kinds other than excess or deficiency of homozygotes. A general method

for testing directly whether homozygotes are in excess or deficiency will be given below.

Before this method had been devised, one of us (LEVENE, unpublished) had tested data from fifty samples collected at Mount San Jacinto and Death Valley in California (data in DOBZHANSKY and EPLING 1944, table 9) by the following method.

The chromosomes appearing in a sample were classified into two types: A, the most common chromosome in the sample (usually Standard in these data) and B, all other chromosomes. Larvae were classified as A/A, A/B, and B/B; and χ^2 was computed, based on these three classes. Fifteen of these fifty samples have now been omitted because they included appreciable numbers of adult males. The seven samples from Wildrose A, B, C, and D have been combined into two groups, Wildrose 1939 and Wildrose 1940. Although DOBZHANSKY and EPLING (1944) have recorded apparently significant differences between the samples from the A, B, C and D stations, these stations are sufficiently close relative to the migration radius of a fly (DOBZHANSKY and WRIGHT 1943) to be treated as parts of a single locality. We then have 30 samples which are essentially egg samples and give the following results. There are 5 samples giving χ^2 values from 0 to .0642, 8 from .0643 to .2749, 4 from .2750 to .7083, 7 from .7084 to 1.642, and 6 greater than 1.642. The expected number of χ^2 values in each of these intervals is 6. A test of goodness of fit on this distribution gives $\chi^2 = 1.667$ with 4 degrees of freedom, or $P = .79$. A more sensitive test is obtained by adding all 30 χ^2 values. The sum is 29.367 and should have a Chi-square distribution with 30 degrees of freedom, giving $P = .50$. Of the 30 samples, 13 have a deficiency of homozygotes and 17 have an excess, which again conforms to expectation.

This evidence shows clearly that there was no important departure from panmixia in these samples. It should be noted that there is a drawback to the statistical method here used. In fact, A/A larvae are homozygotes, and A/B are heterozygotes; but many of the "homozygous" B/B larvae are actually inversion heterozygotes. However, in view of the clearcut nature of the results, it was not felt necessary to undertake the considerable labor of recomputing this material by the new method given below.

STATISTICAL TREATMENT OF ADULT MALE SAMPLES

Since we are now assured that there is a good approach to panmixia, it is of interest to examine adult male samples for evidence of selection. Since egg samples based on impregnated females require much less labor in the laboratory than the analysis of adult males, most of the earlier samples were exclusively egg samples, or contained, at best, relatively few adult males. Since 1945 several larger samples of adult males have been taken for the express purpose of investigating selection. Since it was expected that natural selection would lead to a deficiency of homozygotes, it became desirable to find a method that was specifically designed to test this hypothesis and one that could make use of data from small samples. This method is as follows:

Let h_r be the observed number of homozygotes in the r -th sample, let H_r be

the expected value of h_r and let σ_r be the standard error of h_r . Then if we sum the values of h_r from a number of independent samples of size n_r , the total number of homozygotes $h = \Sigma h_r$ will have expected value ΣH_r and standard error $\sqrt{\Sigma \sigma_r^2}$. Furthermore, h will be nearly normally distributed if h and $\Sigma n_r - h$ are both large, even if the individual sample sizes n_r are small. We can thus consider

$$(1) \quad t = \frac{\Sigma h_r - \Sigma H_r}{\sqrt{\Sigma \sigma_r^2}}$$

as a normal deviate, and reject the hypothesis that the HARDY-WEINBERG equilibrium holds if $P \leq .05$ or some other conventional level of significance, where

$$P = \int_{-\infty}^t \frac{1}{\sqrt{2\pi}} e^{-x^2/2} dx$$

can be obtained from a table of the normal curve (e.g. for $t = -1.64485$, $P = .05$). Note that only negative t are significant since we are only interested in the alternative hypothesis of too few homozygotes. For a large sample $t_r = (h_r - H_r)/\sigma_r$ will itself be normal and can be used to test that particular sample. For simplicity we now drop the subscript r and consider a single unique sample. Suppose there are k distinct inversions present. Let q_i be the *population* frequency of the i -th arrangement, and let y_i be the number of such chromosomes in our sample. Then $\Sigma q_i = 1$ and $\Sigma y_i = 2n$. Also let x_{ii} be the number of homozygous i/i individuals and x_{ij} the number of i/j heterozygotes in the sample. Then if the q_i were known, we would have $E(x_{ii}) = nq_i^2$, $E(x_{ij}) = 2nq_iq_j$, and $E(h) = H = \Sigma nq_i^2$, where $h = \Sigma x_{ii}$ is the number of homozygotes observed and the symbol E stands for "expected value of." Actually, however, the q_i are not known. Hence we must consider the conditional zygotic distribution in samples that have the same number of chromosomes of each type as the observed sample. It can be shown that under these conditions, the exact expected value of x_{ii} is given by

$$E(x_{ii}) = \frac{y_i^2 - y_i}{4n - 2},$$

and hence

$$(2) \quad E(h) = H = \Sigma \frac{y_i^2 - y_i}{4n - 2} = \frac{1}{4n - 2} \{C - 2n\},$$

where

$$C = \Sigma y_i^2.$$

For a single moderate sized sample we could use the approximate formula $E(x_{ii}) = y_i^2/4n$ which corresponds to that when q_i is known, but this would lead to serious bias in combining data from a large number of small samples. Note that when $y_i = 1$ the approximate formula gives $E(x_{ii}) = 1/4n$, while the

exact formula gives $E(x_i) = 0$ correctly, since a homozygous i/i individual requires two i chromosomes. It can also be shown that to a good degree of approximation we have

$$(3) \quad \sigma_h^2 = \frac{1}{4n^2} \left\{ C(n+2) + C^2 \left(\frac{2n+5}{8n^2} \right) - D \frac{n+2}{n} \right\} - \frac{1}{2}$$

where

$$C = \Sigma(y_i^2) \quad \text{and} \quad D = \Sigma(y_i^3).$$

Proofs of the relations (2) and (3) will be published elsewhere (LEVENE, 1949). It should be noted that relation (3) is not exact for small samples, but the error is of the order of magnitude of $1/n$ and, unlike a small error in H , will not become important when many small samples are summed.

We have still to correct for the small error due to failure to observe both chromosomes of some male heterozygotes (see above). Consider ST/CH heterozygotes. In the long run, for every 64 ST/CH flies observed (in data since 1945) we will classify 62 as ST/CH, 1 as ST/ST and 1 as CH/CH. Accordingly we must correct our data by subtracting one ST/ST and one CH/CH and adding two ST/CH flies for every 62 ST/CH actually recorded. In the present case we have h homozygotes and $(n-h)$ heterozygotes recorded, and we have merely to use as our corrected figures

$$(4) \quad \begin{aligned} (n - h^*) &= (n - h) + e, \\ h^* &= h - e, \end{aligned}$$

where $e = \frac{1}{3}(n-h)$ in data before 1945, and $e = \frac{1}{3T}(n-h)$ in data collected during and after 1945. As a result of the correction h^* will occasionally be negative. If we were dealing with a single sample, h^* would then be taken as zero, but in combining a large number of samples bias will result unless the negative values are retained. The random error of classification will not affect the expected value H , but it will increase the variance of h^* . However, it is easy to show that this increase will be approximately equal to e . For our purposes it will then be sufficient to use the formula

$$(5) \quad \sigma^2 = \sigma_{h^*}^2 = \sigma_h^2 + e.$$

Ordinarily this correction will not change σ^2 very much.

As an example of the calculations required, consider the sample from Piñon Flats, June 1946. There were 7 ST/ST, 5 AR/AR, 19 CH/CH, 1 TL/TL, 20 ST/AR, 22 ST/CH, 25 AR/CH, 3 ST/TL, 5 AR/TL, and 4 CH/TL, giving $n = 111$ flies, of which 32 were homozygotes. The calculations are given in table 1. There is a deficiency of homozygotes. The probability of obtaining fewer homozygotes for a sample of 111 with the observed numbers of the given chromosomes, is $P = .185$, and so this sample shows no significant deviation from the equilibrium proportions.

TABLE 1

Computations for Piñon Flats, June 1946. ST=Standard, AR=Arrowhead, CH=Chiricahua, TL=Tree Line. y_i =no. of i chromosomes observed. $Ex_{ii}=(y_i^2-y_i)/(4n-2)$ =no. of i/i homozygotes expected.

CHROMOSOME ARRANGEMENT	i	y_i	y_i^2	y_i^3	$y_i^2-y_i$	Ex_{ii}
ST	1	59	3481	205379	3422	7.7421
AR	2	60	3600	216000	3540	8.0090
CH	3	89	7921	704969	7832	17.7195
TL	4	14	196	2744	182	0.4118
Total		222	15198	1129092	14976	33.8824
		=2n	=C	=D		=H

$$n = 111, \quad h = 32, \quad n - h = 79, \quad 4n - 2 = 442,$$

$$e = (n - h)/31 = 79/31 = 2.5484, \quad h^* = h - e = 29.4516,$$

$$H = (C - 2n)/(4n - 2) = (15198 - 222)/442 = 33.8824 \text{ check,}$$

$$\sigma_h^2 = \frac{1}{4n^2} \left\{ C(n+2) + C^2 \frac{2n+5}{8n^2} - D \frac{n+2}{n} \right\} - \frac{1}{2}$$

$$= \frac{1}{49284} \left\{ 15198 \times 113 + \frac{230979204 \times 227}{98568} - \frac{1129092 \times 113}{111} \right\} - \frac{1}{2}$$

$$= 22.3171 - \frac{1}{2} = 21.8171,$$

$$\sigma^2 = \sigma_h^2 + e = 21.8171 + 2.5484 = 24.3655, \quad \sigma = 4.9361$$

$$t = \frac{h^* - H}{\sigma} = \frac{29.4516 - 33.8824}{4.9361} = -0.8976,$$

$$P = \int_{-\infty}^{-0.8976} \frac{1}{\sqrt{2\pi}} e^{-x^2/2} dx = 0.1847.$$

DEPARTURE FROM EQUILIBRIUM IN ADULT MALE SAMPLES

Table 2 summarizes the data for 66 adult male samples that have been analyzed. The size of the samples ranged from 5 to 279 individuals, with only five samples having more than 100 individuals each. In table 2, the locality and date of the samples are given in the two columns on the left, followed by size of the sample (number of males analyzed), number of homozygous individuals found, corrected number of homozygotes, expected number of homozygotes, and the variance (σ^2).

The analysis can be started by observing that in 56 samples the observed numbers of homozygotes are less than the expected ones, while in only 10 samples is the relationship reversed. If no differential mortality of inversion homo- and heterozygotes occurs in natural populations between the egg stage and the stage at which the adult males are captured, positive and negative deviations should be about equally frequent. This suggests a real deficiency of homozygotes in the natural populations sampled. Among the ten largest samples (with more than 50 flies each), all show fewer homozygotes than ex-

TABLE 2

Individual adult male samples. n = no. of males analyzed. h = no. of homozygotes. h^* = corrected no. of homozygotes. H = no. of homozygotes expected under HARDY-WEINBERG equilibrium. σ^2 = variance of h^* .

LOCALITY	DATE	n	h	h^*	H	σ^2
Andreas	May 39	30	17	16.794	13.169	4.769
"	June 39	17	5	4.809	5.121	3.359
"	Apr. 41	23	10	9.794	11.822	2.718
"	Apr. 42	22	13	12.857	12.163	2.227
"	Apr. 20/40	24	12	11.819	12.276	3.083
"	Oct. 39	16	3	2.794	5.516	2.708
"	Nov. 39	34	11	10.635	14.343	6.109
"	Dec. 39	22	8	7.778	10.070	3.412
"	Jan. 40	18	4	3.778	6.514	3.469
"	Feb. 40	22	8	7.778	10.930	4.328
"	Mar. 40	15	8	7.889	8.276	1.339
"	Mar. 41	22	10	9.809	12.442	2.722
"	Mar. 42	25	12	11.794	13.551	3.664
"	Oct. 40	20	10	9.841	9.846	3.990
"	Mar. 28/40	16	4	3.809	5.129	3.690
"	Sept. 6/41	29	13	12.746	14.333	3.933
"	Feb. 19/41	23	10	9.794	10.822	3.262
"	Feb. 1/41	12	5	4.889	6.304	1.417
Piñon	May 39	15	4	3.825	4.897	3.225
"	Apr. 40	40	8	7.492	11.911	8.602
"	June 40	19	7	6.809	5.838	4.131
"	Apr. 45	63	18	16.548	20.016	14.745
"	June 46	111	32	29.452	33.882	24.366
"	Apr. 47	111	38	35.645	37.195	23.709
"	Sept. 39	7	0	-0.111	2.154	1.621
"	Oct. 39	15	3	2.809	5.621	3.078
"	Mar. 40	9	0	-0.143	3.059	1.816
"	Dec. 41	20	9	8.825	7.718	3.740
"	Mar. 46	279	106	100.419	108.546	49.415
"	1940	14	4	3.841	4.148	3.002
Keen	May 39	8	2	1.805	2.600	1.822
"	June 39	38	7	6.508	12.173	8.651
"	July 39	23	3	2.682	7.444	5.382
"	Sept.-Oct. 39	15	1	0.778	4.758	3.227
"	July 40	15	2	1.794	5.241	3.212
"	Aug. 40	36	8	7.556	12.394	8.042
"	Sept. 40	22	5	4.730	7.232	2.491
"	Apr. 40	35	8	7.571	12.203	7.771
"	Apr. 45	50	16	14.903	14.141	10.609
"	Apr. 46	134	46	43.161	48.285	25.634
Mather	May 47	15	3	2.613	4.690	3.708
"	Sept. 47	114	21	18.000	30.318	23.409
Aspen	Sept. 47	9	2	1.774	2.176	1.760
Lost Claim	Aug. 46	31	8	7.258	9.836	6.745
"	May 47	10	2	1.742	3.421	2.266
"	Sept. 47	5	0	-0.161	1.111	1.036
Avawatz Mt.	May 39	14	4	3.841	6.407	2.180

TABLE 2—(continued)

LOCALITY	DATE	n	h	h*	H	σ^2
Coso Mt.	July 37	36	21	20.762	21.394	3.860
Charleston Mt.	June 39	24	15	14.857	13.468	2.631
Cottonwood Mt.	June 37	68	23	22.286	27.363	15.143
Grapevine Mt.	June 37	29	9	8.682	12.132	6.055
Kingston Mt.	May 37	40	22	21.714	22.633	4.929
Lida Nev.	June 37	29	19	18.841	18.702	2.088
Panamint Mt.	May 37	46	21	20.603	24.253	6.108
Providence Mt.	May 37	54	41	40.794	42.065	1.632
Sheep Range	June 37	58	44	43.778	45.470	2.477
Wildrose	Sept. 38	20	8	7.809	5.974	3.954
"	June 39	89	27	26.016	32.254	19.617
"	1940	25	9	8.746	8.428	5.247
Jacksonville	June 46	16	4	3.613	5.387	3.237
"	July 46	15	5	4.677	5.897	2.193
"	Sept. 47	22	9	8.581	7.535	3.915
Raton	1940	32	21	20.825	22.587	2.365
Santa Cruz	1940	21	6	5.762	6.634	3.926
Santa Lucia	1940	16	4	3.809	5.903	2.598
Sonoma	1941	12	3	2.857	4.565	2.692

pected. Nevertheless, in only one sample (taken at Mather, California, in September 1947) is the deviation significant by the usual criteria ($P = .0054$); for the other nine the P values range from .375 to .051.

The critical evidence comes from adding the values of deviations and variances from different samples as described above. We then find for the ten largest samples the deviation $h^* - H = -50.30$ and $\sigma = 14.15$ corresponding to a P value of .0002, while for all 66 samples $h^* - H = -139.30$, $\sigma = 20.35$ and P is less than 10^{-6} . The conclusion is justified that inversion homozygotes are significantly less frequent, and heterozygotes more frequent, in natural populations than they would be if no differential mortality occurred between the egg stage and the stage of capture.

Since the present data result from combining samples from widely scattered times and places, with considerable differences in numbers and relative proportions of the different chromosome types, there is no satisfactory over-all measure of the deviation from the HARDY-WEINBERG equilibrium. However, for a rough indication it may be noted that for the combined data the ratio $(\Sigma h^* - \Sigma H) / \Sigma H = -.147$, or there is a 14.7% deficiency of homozygotes. The lack of a good measure of the extent of the deviation does not interfere with the combination of the data for purposes of the test of significance.

Table 3 represents an unsuccessful attempt to group the adult male samples in categories which could be compared with the known facts about seasonal changes in the frequencies of gene arrangements. Thus, seasonal changes have been recorded at Andreas Canyon and at Piñon Flats, but not at Keen Camp on Mount San Jacinto. Changes occur in spring and summer but not in winter (DOBZHANSKY 1943). Seasonal changes have been recorded in the Sierra Ne-

vada, and changes from year to year are indicated for some localities in the Death Valley region (DOBZHANSKY and EPLING 1944, DOBZHANSKY 1948). The population of Keen underwent considerable change between 1940 and 1945 (DOBZHANSKY 1947b). P values which indicate significant deficiencies of homozygotes appear in table 3 for early samples at Keen Camp, for winter samples in Andreas Canyon, for the Sierra Nevada, for Death Valley, winter samples at Piñon Flats, and miscellaneous samples. Summer samples from

TABLE 3

Results of adult male samples grouped together (see text). n =no. of males analyzed. h =no. of homozygotes. h^* =corrected no. of homozygotes. H =no. of homozygotes expected under HARDY-WEINBERG equilibrium. σ^2 =variance of h^* . $t=(h^*-H)/\sigma$. P =probability of as many or fewer homozygotes if HARDY-WEINBERG equilibrium holds (see text).

DESCRIPTION	n	h	h^*	H	σ^2	t	P
Andreas Summer	116	57	56.073	54.551	16.156	+0.3789	0.6476
Andreas Winter	274	106	103.334	128.076	44.043	-3.7279	0.0001
Piñon Summer	359	107	99.771	113.739	78.778	-1.5737	0.0578
Piñon Winter	344	122	115.640	131.246	62.672	-1.9711	0.0243
Keen to 1940	192	36	33.424	64.045	40.598	-4.8056	<10 ⁻⁶
Keen 1945-6	184	62	58.064	62.426	36.243	-0.7246	0.2344
Sierra Nevada	184	36	31.226	51.552	38.924	-3.2579	0.0006
Death Valley	532	263	258.729	281.543	75.921	-2.6184	0.0044
Miscellaneous	134	52	50.124	58.508	20.926	-1.8330	0.0334
Total	2319	841	806.385	945.686	414.261	-6.8442	<10 ⁻⁶

Piñon Flats gave a P value of about 0.058, while no significant deviation is indicated from the recent Keen samples, and the summer samples from Andreas Canyon contain even an insignificant excess of homozygotes. No conclusion can be drawn about the relationships between the observed deficiencies of homozygotes and the known seasonal changes in the incidence of gene arrangements. It should be noted that while the total sample size is adequate for our purposes, the number of flies in the separate groups is too small to permit satisfactory conclusions to be drawn about them.

DISCUSSION

The purpose of the present study has been to test the hypothesis that the frequencies in natural populations of gene arrangements in the third chromosome of *Drosophila pseudoobscura* are controlled by natural selection. As stated in the Introduction, this hypothesis was originally advanced on the basis of observations on seasonal changes in the frequencies of the chromosomal types in certain localities (DOBZHANSKY 1943). This hypothesis was first confirmed by experiments which showed that some of the changes observed in nature can be reproduced in artificial populations in population cages (WRIGHT and DOBZHANSKY 1946). Next, it was shown that, in population cages, there is a differential mortality between the egg and the adult stage which favors inver-

sion heterozygotes and discriminates against homozygotes (DOBZHANSKY 1947a). The data reported in the present article complete the proof of the hypothesis by showing that for the eggs deposited in natural populations the proportions of homo- and heterozygotes are as demanded by the HARDY-WEINBERG rule, while among the adult males found in nature heterozygotes are more, and homozygotes are less, frequent than this rule requires. It follows that, at least among the male zygotes, there is differential mortality which favors inversion heterozygotes. This fact alone, without any information on seasonal or other temporal changes, would be sufficient to show that the frequencies of the gene arrangements in nature are subject to selective pressure.

SUMMARY

In wild populations of *Drosophila pseudoobscura*, the proportions of homozygotes and heterozygotes for different types of third chromosomes are, among the eggs deposited by the adult flies, in conformity with the binomial square rule (the HARDY-WEINBERG formula). Yet, among the adult male flies found in nature these proportions depart from the binomial square rule, because the homozygotes are less, and heterozygotes more, frequent than demanded by the rule. Thus, a differential mortality occurs between the egg and the adult stage which favors the heterozygotes. The chromosomal variation is controlled by natural selection.

LITERATURE CITED

- DOBZHANSKY, TH., 1943 Genetics of natural populations. IX. Temporal changes in the composition of populations of *Drosophila pseudoobscura*. *Genetics* **28**: 162-186.
1947a Genetics of natural populations. XIV. A response of certain gene arrangements in the third chromosome of *Drosophila pseudoobscura* to natural selection. *Genetics* **32**: 142-160.
1947b A directional change in the genetic constitution of a natural population of *Drosophila pseudoobscura*. *Heredity* **1**: 53-64.
1948. Genetics of natural populations. XVI. Altitudinal and seasonal changes produced by natural selection in certain populations of *Drosophila pseudoobscura* and *Drosophila persimilis*. *Genetics* **33**: 158-178.
- DOBZHANSKY, TH., and C. EPLING, 1944. Contributions to the genetics, taxonomy and ecology of *Drosophila pseudoobscura* and its relatives. Carnegie Inst. Washington Publ. **554**: 1-183.
- DOBZHANSKY, TH., and S. WRIGHT, 1943 Genetics of natural populations. X. Dispersion rates in *Drosophila pseudoobscura*. *Genetics* **28**: 304-340.
- LEVENE, H., 1949 On a matching problem arising in Genetics. *Ann. Math. Statistics* **20** (in press).
- WRIGHT, S., and TH. DOBZHANSKY, 1946 Genetics of natural populations. XII. Experimental reproduction of some of the changes caused by natural selection in certain populations of *Drosophila pseudoobscura*. *Genetics* **31**: 125-156.

ON THE MATHEMATICS OF RANDOM MATING IN CASE OF
DIFFERENT RECOMBINATION VALUES FOR
MALES AND FEMALES

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In a colloquium discussion PROFESSOR SEWALL WRIGHT remarked that cases where the recombination values (r.v.'s) are different for the two sexes appear so common that the mathematical theory should be completely worked out. He added that in case of *two* and *three* Mendelian characters the arithmetic mean $(c+d)/2$ of the two r.v.'s plays the role of the single r.v. appearing in the usual situation where one and the same recombination value, c , holds for males and for females.

In the following the mathematics of the problem is completely given. The result is that Professor WRIGHT'S statement is true for any number of characters. More specifically: In case of $m=2$ or of $m=3$ characters we have an unrestricted analogy to the "ordinary" case. If $m \geq 4$ the situation changes. The general character of the problem will, however, still be determined by the mean of the r.v.'s. This is, in particular, true for the limit behaviour of the distributions as n , the number of distinct generations, tends toward infinity.

As in previous papers (GEIRINGER 1944, 1945) the author's approach is based on the consideration of three basic *probability distributions*, the *distribution of genotypes*, (d. ge.), the *distribution of gametes*, (d. ga.), and the *linkage distribution* (l.d.). If the first is given for an "initial" generation for both sexes, if we know or assume a l.d., and if random mating is considered we may derive the d. ga. for the initial generation, and both the d. ge. and the d. ga. for any subsequent generation ($n=0, 1, 2, \dots$). Mathematically, the problem appears as a probability problem. To the not mathematically minded biologist this may seem a non customary approach. If however the usual way of formation of abstract concepts in science is used it will be realized that these "proportions" or "frequencies" of certain types have to be regarded as probabilities and probability distributions. The consideration of such distributions affords the best way to deal with more involved heredity situations since it enables us to use the highly developed methods and concepts of probability calculus.

In sections 1 and 2 of this paper the cases of $m=2$ and $m=3$ characters are completely investigated with details which seem not obvious. In each case we first derive the "recurrence formula" [(16) in sec. 1 and (31) in sec. 2] which enable us to compute the characteristic distributions from generation to generation. The result is that, indeed, from the first filial generation on, the recurrence relations are exactly the same as in the "ordinary" case with the arithmetic mean of the corresponding r.v.'s and the arithmetic mean of the corresponding gametic probabilities taking the place of the r.v.'s and of the gametic distribution of the "ordinary" case.—Next, we solve the recurrence equations

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(mathematically they are "difference" equations), that means we derive expressions which give the distribution in the n^{th} generation directly in terms of the initial distribution and of the given r.v.'s [(18) and (33)]. Finally, by means of these last formulae the *limit distribution* as $n \rightarrow \infty$ is easily found [(20), (37), and (38)].

In section 3 about the same is done for general $m \geq 4$. Here a general l.d., or rather two such distributions in our case, take the place of the three pairs of r.v.'s which appear if $m = 3$. The recurrence relations are not quite of the aforementioned type but the limit theorem is still the expected analogon to the simpler case. It is derived directly from the recurrence formula.

There would be no worthwhile simplification if we restrict ourselves to *two* alleles (dominant and recessive; A and a). Hence an *arbitrary number of alleles*, r , is assumed throughout.

1. *The problem in case of $m = 2$ loci.*

Call m the number of Mendelian characters, r the number of alleles under consideration, and begin with the case of $m = 2$ and $r = 2$. There are 16 possible genotypes. It has been found an essential advantage to denote, quite generally, the genotype of an individual in a way which shows clearly the maternal and the paternal heritage. If the two possibilities are denoted by A, a and B, b respectively, the 16 types follow, the letters before the semicolon denoting the maternal heritage:

(AB; AB)	(AB; Ab)	(AB; aB)	(AB; ab)
(Ab; AB)	(Ab; Ab)	(Ab; aB)	(Ab; ab)
(aB; AB)	(aB; Ab)	(aB; aB)	(aB; ab)
(ab; AB)	(ab; Ab)	(ab; aB)	(ab; ab)

If we denote briefly the whole maternal heritage by x and the paternal one by y we assume, as usual, that the genotypes $(x; y)$ and $(y; x)$ are the same:

$$(1) \quad (x; y) = (y; x)$$

(that means for example that $(AB; Ab) = (Ab; AB)$). Hence in the above scheme the types symmetrical to the "main diagonal" are the same, which reduces the maximum number of different types from 16 to 10.

If we consider r alleles and m characters the number $N = r^{2m}$ takes obviously the place of $N = 2^4 = 16$ while $r^m(r^m + 1)/2 = N_1$ takes the place of $2^2(2^2 + 1)/2 = 10$.

Returning to our particular case, each of the 16 types will initially occur in certain proportions. These proportions will, in general, change from generation to generation. We thus introduce the probability *distribution of genotypes*, $w^{(n)}(x; y)$ in the n^{th} generation where x and y stand for the total maternal and paternal heritage respectively. In accordance with (1) we have to assume that

$$(2) \quad w^{(n)}(x; y) = w^{(n)}(y; x) \quad (n = 0, 1, \dots).$$

Since $w^{(n)}(x; y)$ is a probability distribution we have

$$(3) \quad \sum_x \sum_y w^{(n)}(x; y) = 1:$$

In our particular case, $m=r=2$, we have

$$w^{(n)}(AB; AB) + [w^{(n)}(AB; Ab) + w^{(n)}(Ab; AB)] + \dots + w^{(n)}(ab; ab) = 1.$$

We may now assume that the initial distributions of genotypes are different for males and females. (This is not an essential assumption since after one generation of random mating the d. ge. will be the same for both sexes. See (7)). Let $\omega^{(0)}(x; y)$ be the initial distribution for the females, $\omega^{(0)}(x; y)$ that for the males. Then we have, besides (2) and (3)

$$(2') \quad \begin{aligned} w^{(0)}(x; y) &= w^{(0)}(y; x), \\ \sum_x \sum_y \omega^{(0)}(x; y) &= 1. \end{aligned}$$

If $m=r=2$ four different gametes are possible: (AB), (Ab), (aB), and (ab). They appear in proportions given by the probability *distribution of gametes* which in our problem will be a different one for the two sexes. It will be denoted by $p^{(n)}(AB)$, \dots and by $q^{(n)}(AB)$, \dots and we have

$$(4) \quad p^{(n)}(AB) + p^{(n)}(Ab) + p^{(n)}(aB) + p^{(n)}(ab) = 1$$

$$(4') \quad q^{(n)}(AB) + q^{(n)}(Ab) + q^{(n)}(aB) + q^{(n)}(ab) = 1.$$

In case of random mating the d.ga. is derived from the d.ge. by means of the segregation distribution. The s.d. specifies the kinds of gametes an organism can produce. This s.d., or, as we shall call it, this *linkage distribution*, (l.d.), is trivial in case of $m=1$ character, and fairly simple in case of $m=2$, but not so simple for general m . If $m=1$, and $r=2$ the three different genotypes are (A; A), (A; a), (a; a). (The semicolon is unnecessary if $m=1$.) We may denote the d.ge. by $w^{(n)}(AA) = p_n$, $w^{(n)}(Aa) = 2q_n$, $w^{(n)}(aa) = r_n$ and the d.ga. by $p^{(n)}(A) = u_n$, $p^{(n)}(a) = v_n$. We then have obviously: $u_n = p_n \cdot 1 + 2q_n \cdot \frac{1}{2}$, $v_n = 2q_n \cdot \frac{1}{2} + r_n \cdot 1$. We see that the l.d. is here simply given by the factors 1 and $\frac{1}{2}$ respectively. In fact, an individual which is of type (AA) transmits A with a probability of 1, while the individual of type (Aa) transmits A with a probability of $\frac{1}{2}$, and so on.

If $m=2$, the l.d. in the "ordinary" case is completely characterized by *one* parameter, the *recombination value* (r.v.). With a view to later considerations for general m we may describe the mathematical situation as follows: The individual may transmit a gamete consisting of: a) both "maternal" genes, b) the "maternal" gene with respect to the first character, and with respect to the second character the "paternal" gene, c) with respect to the first character the "paternal," and with regard to the second the "maternal" gene, d) both "paternal" genes. (This "schematic" probability explanation is independent of "linear theory" or "chiasma theory," and it need not be modified if "chromatid segregation" rather than "chromosome segregation" is taken into account.) The probability that either b) or c) will happen is denoted by c , and that for a) or d) accordingly by $(1-c)$. More specifically $c/2$ is the probability of the

"event" b) and likewise of the event c), and so on. This obviously applies to any number of alleles since we have merely spoken of "paternal" and "maternal" genes with respect to a character no matter by what gene this character is represented.

In our problem we now assume that this parameter, the r.v., is *not the same* for the two sexes; we shall call it *c* for the females and *d* for the males.

We shall now derive the initial d.g.a. from the initial d.g.e. by means of our s.d. (or l.d.). We begin with the probability $p^{(0)}(AB)$ of a female gamete and obtain as will be explained:

$$\begin{aligned}
 p^{(0)}(AB) &= w^{(0)}(AB; AB) \cdot 1 + [w^{(0)}(AB; Ab) \cdot \frac{1}{2} + w^{(0)}(Ab; AB) \cdot \frac{1}{2}] \\
 &\quad + [w^{(0)}(AB; aB) \cdot \frac{1}{2} + w^{(0)}(aB; AB) \cdot \frac{1}{2}] \\
 (5) \quad &\quad + \left[w^{(0)}(Ab; aB) \cdot \frac{c}{2} + w^{(0)}(aB; Ab) \cdot \frac{c}{2} \right] \\
 &\quad + \left[w^{(0)}(AB; ab) \cdot \frac{1-c}{2} + w^{(0)}(ab; AB) \cdot \frac{1-c}{2} \right].
 \end{aligned}$$

To understand this let us first remember that a gamete (AB) can be formed only by a parent which 1) possesses A and B and 2) also transmits these genes. Consider, then, for example, the term $w^{(0)}(AB; Ab) \cdot \frac{1}{2}$. This is the probability that an individual be of type (AB; Ab) times the probability to transmit AB; this last probability equals $\frac{1}{2}$, since A will be transmitted anyway and B (rather than b) with probability $\frac{1}{2}$. Likewise the term, $w^{(0)}(Ab; aB) \cdot c/2$ is the probability that the parent be of type (Ab; aB) and transmits the "mixed" gamete AB which consists of the "maternal" A, and the "paternal" B, and this "recombination" happens with probability $c/2$.

A completely analogous formula holds for males:

$$\begin{aligned}
 q^{(0)}(AB) &= \omega^{(0)}(AB; AB) \cdot 1 + [(\omega^{(0)}(AB; Ab) \frac{1}{2} + \omega^{(0)}(Ab; AB) \frac{1}{2}) \\
 (6) \quad &\quad + \left[\omega^{(0)}(AB; ab) + \omega^{(0)}(ab; AB) \right] \frac{1-d}{2}.
 \end{aligned}$$

Next, we remember that a new organism is formed by the fusion of two gametes. If everything happens at random this amounts to the principle:

$$(7) \quad w^{(n+1)}(x; y) = p^{(n)}(x)q^{(n)}(y) \quad (n = 0, 1, \dots).$$

In fact a zygote whose maternal and paternal heritages are *x* and *y* respectively is formed by the fusion of the egg which contributes *x* and the sperm of type *y* and the probability of such a zygote is consequently given by (7) where $p^{(n)}(x)$ and $q^{(n)}(y)$ are the respective female and male gene probabilities. For instance, $w^{(n+1)}(AB; Ab) = p^{(n)}(AB)q^{(n)}(Ab)$. ($n = 0, 1, \dots$).

A formula analogous to (5) and (6) holds for $n = 1, 2, \dots$. In order to obtain a general recurrence relation we write

$$p^{(n+1)}(AB) = w^{(n+1)}(AB; AB) \cdot 1 + [w^{(n+1)}(AB; Ab) \frac{1}{2} + w^{(n+1)}(Ab; AB) \cdot \frac{1}{2}$$

$$(5') \quad + \dots + \left[w^{(n+1)}(Ab; aB) \frac{c}{2} + w^{(n+1)}(aB; Ab) \cdot \frac{c}{2} \right]$$

and there is a formula (6') for $q^{(n+1)}(AB)$ which is like (5') with the only difference that the r.v. is now d rather than c . Substituting (7) into (5') we obtain

$$(8) \quad \begin{aligned} p^{(n+1)}(AB) &= p^{(n)}(AB)q^{(n)}(AB) \\ &+ [p^{(n)}(AB)q^{(n)}(Ab) + p^{(n)}(Ab)q^{(n)}(AB)] \cdot \frac{1}{2} \\ &+ [p^{(n)}(AB)q^{(n)}(aB) + p^{(n)}(aB)q^{(n)}(AB)] \cdot \frac{1}{2} \\ &+ [p^{(n)}(AB)q^{(n)}(ab) + p^{(n)}(ab)q^{(n)}(AB)] \cdot \frac{1-c}{2} \\ &+ [p^{(n)}(Ab)q^{(n)}(aB) + p^{(n)}(aB)q^{(n)}(Ab)] \cdot \frac{c}{2} \end{aligned}$$

($n = 0, 1, 2, \dots$)

and an analogous formula for $q^{(n+1)}(AB)$ in terms of $p^{(n)}$, $q^{(n)}$, and d . There are also formulae like (8) for $p^{(n+1)}(Ab)$, for $p^{(n+1)}(aB)$, for $p^{(n+1)}(ab)$ and the like for the $q^{(n+1)}$. Such a formula already constitutes a recurrence formula since it shows how to find $p^{(n+1)}$ from the distributions for the n th generation. All it needs is to be transformed so as to exhibit a clear structure.

For this purpose we introduce the *gene-probabilities* (in probability calculus called "marginal distributions") namely:

$$(9) \quad \begin{aligned} p_1^{(n)}(A) &= p^{(n)}(AB) + p^{(n)}(Ab), & p_1^{(n)}(a) &= p^{(n)}(aB) + p^{(n)}(ab) \\ p_2^{(n)}(B) &= p^{(n)}(AB) + p^{(n)}(aB), & p_2^{(n)}(b) &= p^{(n)}(Ab) + p^{(n)}(ab) \end{aligned}$$

for $n=0, 1, \dots$. Here $p_1^{(n)}(A)$ is the probability of the gene A , and so forth, and we have

$$(9') \quad p_1^{(n)}(A) + p_1^{(n)}(a) = 1, \quad p_2^{(n)}(B) + p_2^{(n)}(b) = 1, \quad (n = 0, 1, \dots).$$

We introduce in the same way for the males: $q_1^{(n)}(A), \dots, q_2^{(n)}(b)$. Using these definitions as well as (4) and (4') we find by an elementary computation that the right side of (8) equals

$$\frac{1-c}{2} [p^{(n)}(AB) + q^{(n)}(AB)] + \frac{c}{2} [p_1^{(n)}(A)q_2^{(n)}(B) + q_1^{(n)}(A)p_2^{(n)}(B)]$$

and we get the two formulae

$$\begin{aligned} p^{(n+1)}(AB) &= \frac{1-c}{2} [p^{(n)}(AB) + q^{(n)}(AB)] \\ &+ \frac{c}{2} [p_1^{(n)}(A)q_2^{(n)}(B) + q_1^{(n)}(A)p_2^{(n)}(B)] \\ q^{(n+1)}(AB) &= \frac{1-d}{2} [p^{(n)}(AB) + q^{(n)}(AB)] \end{aligned}$$

$$+ \frac{d}{2} [p_1^{(n)}(A)q_2^{(n)}(B) + q_1^{(n)}(A)p_2^{(n)}(B)].$$

In the same way we obtain formulae for $p^{(n+1)}(Ab)$, $p^{(n+1)}(aB)$, $p^{(n+1)}(ab)$, \dots , $q^{(n+1)}(ab)$.

Next we add the formula for $p^{(n+1)}(AB)$ and that for $p^{(n+1)}(Ab)$. Using (9') we find

$$(11) \quad p_1^{(n+1)}(A) = \frac{1-c}{2} [p_1^{(n)}(A) + q_1^{(n)}(A)] + \frac{c}{2} [p_1^{(n)}(A) + q_1^{(n)}(A)] \\ = \frac{1}{2} [p_1^{(n)}(A) + q_1^{(n)}(A)], \quad (n = 0, 1, \dots)$$

and in the same way

$$(11') \quad q_1^{(n+1)}(A) = \frac{1}{2} [p_1^{(n)}(A) + q_1^{(n)}(A)], \quad (n = 0, 1, \dots).$$

Comparing (11) and (11') we see the interesting fact that $p_1^{(n+1)}(A) = q_1^{(n+1)}(A)$, for $n=0, 1, \dots$ or, since the same holds for the other genes:

$$q_1^{(n)}(A) = p_1^{(n)}(A), \quad q_1^{(n)}(a) = p_1^{(n)}(a), \dots, \quad q_2^{(n)}(b) = p_2^{(n)}(b), \\ (n = 1, 2, \dots)$$

while the $q^{(n)}(A, B)$ are not equal to the $p^{(n)}(AB)$, and so forth. Substituting this in (11) we obtain

$$p_1^{(n+1)}(A) = \frac{1}{2} [p_1^{(n)}(A) + p_1^{(n)}(A)] = p_1^{(n)}(A), \quad (n = 1, 2, \dots)$$

Thus we have for the gene probabilities, for $n=1, 2, \dots$:

$$(12) \quad p_1^{(n)}(A) = p_1^{(1)}(A) = \frac{1}{2} [p_1^{(0)}(A) + q_1^{(0)}(A)] = q_1^{(1)}(A) = q_1^{(n)}(A)$$

$$(12') \quad p_2^{(n)}(B) = p_2^{(1)}(B) = \frac{1}{2} [p_2^{(0)}(B) + q_2^{(0)}(B)] = q_2^{(1)}(B) = q_2^{(n)}(B)$$

and analogous relations for the $p_1^{(n)}(a)$ and $p_2^{(n)}(b)$. If we introduce these results into (10) these formulae simplify. In fact, for $n=1, 2, \dots$

$$p_1^{(n)}(A)q_2^{(n)}(B) + q_1^{(n)}(A)p_2^{(n)}(B) \\ = p_1^{(1)}(A)q_2^{(1)}(B) + q_1^{(1)}(A)p_2^{(1)}(B) = 2p_1^{(1)}(A)p_2^{(1)}(B)$$

and we obtain a first result:

$$(10') \quad p^{(n+1)}(AB) = \frac{1-c}{2} [p^{(n)}(AB) + q^{(n)}(AB)] + c p_1^{(1)}(A) p_2^{(1)}(B) \\ q^{(n+1)}(AB) = \frac{1-d}{2} [p^{(n)}(AB) + q^{(n)}(AB)] + d p_1^{(1)}(A) p_2^{(1)}(B) \\ (n = 1, 2, \dots).$$

Before continuing we wish to state that all this applies in the same way to any number, r , of alleles. In fact, in this case, firstly, the formula (5) will contain some more terms; for instance, if $r=4$ it would start like this:

$$p^{(0)}(a_1 b_1) = w^{(0)}(a_1 b_1; a_1 b_1) \cdot 1 + \frac{1}{2} [w^{(0)}(a_1 b_1; a_1 b_2) + w^{(0)}(a_1 b_1; a_1 b_3) \\ + w^{(0)}(a_1 b_1; a_1 b_4) + \dots]$$

and the same remark holds for (5') and (6). Formula (7) is general. Formula (8) will again contain more terms since it is derived from (5), but the decisive transformation of (8) will lead to exactly the same result as in case $r=2$ since we now have instead of (9) and (9') with an obvious notation, for $i=1, 2, \dots, r$, and $n=0, 1, \dots$:

$$(9') \quad p_1^{(n)}(a_i) = \sum_{j=1}^r p^{(n)}(a_i b_j), \quad p_1^{(n)}(b_i) = \sum_{j=1}^r p^{(n)}(a_j b_i), \\ q_1^{(n)}(a_i) = \sum_{j=1}^r q^{(n)}(a_i b_j), \quad q_2^{(n)}(b_i) = \sum_{j=1}^r q^{(n)}(a_j b_i).$$

It is however simpler to use a slightly different notation, namely to introduce a *variable*, x , which takes on the values a_1, \dots, a_r , and a *variable*, y , which takes on the values b_1, \dots, b_r . Then we simply have

$$(9'') \quad p_1^{(n)}(x) = \sum_y p^{(n)}(xy), \quad p_2^{(n)}(y) = \sum_x p^{(n)}(xy), \\ q_1^{(n)}(x) = \sum_y q^{(n)}(xy), \quad q_2^{(n)}(y) = \sum_x q^{(n)}(xy)$$

with

$$(9''') \quad \sum_x p_1^{(n)}(x) = \sum_y p_2^{(n)}(y) = \sum_x q_1^{(n)}(x) = \sum_y q_2^{(n)}(y) = 1.$$

Also instead of (12) we now write

$$(12'') \quad p_1^{(n)}(x) = p_1^{(1)}(x) = \frac{1}{2} [p_1^{(0)}(x) + q_1^{(0)}(x)] = q_1^{(1)}(x) = q_1^{(n)}(x),$$

$$(12''') \quad p_2^{(n)}(y) = p_2^{(1)}(y) = \frac{1}{2} [p_2^{(0)}(y) + q_2^{(0)}(y)] = q_2^{(1)}(y) = q_2^{(n)}(y) \\ (x = a_1, a_2, \dots, a_r, y = b_1, b_2, \dots, b_r, n = 1, 2, \dots).$$

The generalized formulae corresponding to (10') will now be:

$$p^{(n+1)}(xy) = \frac{1-c}{2} \cdot [p^{(n)}(xy) + q^{(n)}(xy)] + c p_1^{(1)}(x) p_2^{(1)}(y)$$

$$q^{(n+1)}(xy) = \frac{1-d}{2} \cdot [p^{(n)}(xy) + q^{(n)}(xy)] + d p_1^{(1)}(x) p_2^{(1)}(y)$$

$$(x = a_1, \dots, a_r, y = b_1, \dots, b_r, (n = 1, 2, \dots)).$$

In order to prove the statement in the introduction we introduce the distribution

$$(14) \quad r^{(n)}(xy) = \frac{1}{2} [p^{(n)}(xy) + q^{(n)}(xy)], \quad (n = 0, 1, \dots)$$

with

$$(14') \quad \sum_x \sum_y r^{(n)}(xy) = 1.$$

We then obtain, step by step, using (12), (12''), (12'''):

$$\begin{aligned} \sum_y r^{(n)}(xy) &\equiv r_1^{(n)}(x) = \frac{1}{2} [p_1^{(n)}(x) + q_1^{(n)}(x)] \\ &= \frac{1}{2} [p_1^{(1)}(x) + q_1^{(1)}(x)] = p_1^{(1)}(x) = q_1^{(1)}(x) \\ &= \frac{1}{2} [p_1^{(0)}(x) + q_1^{(0)}(x)] = r_1^{(0)}(x), \end{aligned}$$

(n = 0, 1, ...).

Thus, for n=0,1, ...

$$(15) \quad \begin{aligned} r_1^{(n)}(x) &= r_1^{(0)}(x) = p_1^{(1)}(x) = q_1^{(1)}(x) = \frac{1}{2} [p_1^{(0)}(x) + q_1^{(0)}(x)] \\ r_2^{(n)}(y) &= r_2^{(0)}(y) = p_2^{(1)}(y) = q_2^{(1)}(y) = \frac{1}{2} [p_2^{(0)}(y) + q_2^{(0)}(y)]. \end{aligned}$$

If we now add the two formulae (13) and divide by two, we get our *final* elegant result, valid for n=1, 2, ...

$$(16) \quad r^{(n+1)}(xy) = r^{(n)}(xy) \cdot \frac{(1-c) + (1-d)}{2} + r_1^{(0)}(x)r_2^{(0)}(y) \cdot \frac{c+d}{2}.$$

This is exactly the same formula as the usual formula for m=2 (see papers by JENNINGS (1917, 1923), ROBBINS (1918), and the author, l.c.) the only difference being: 1) that $r^{(n)}(xy) = \frac{1}{2} \cdot [p^{(n)}(xy) + q^{(n)}(xy)]$ takes the place of $p^{(n)}(xy)$. 2) $\frac{1}{2} \cdot (c+d)$ takes the place of c. 3) It holds for n=1, 2, ... only, not for n=0, 1, ...

Since (16) holds from n=1 on only, it has to be completed by the direct computation of the first step in order to find $r^{(1)}(xy)$. For this purpose we must return to (10) and find, for n=0, upon addition of the two formulae (10) and dividing by $\frac{1}{2}$:

$$(16') \quad \begin{aligned} r^{(1)}(xy) &= \frac{(1-c) + (1-d)}{2} r^{(0)}(xy) \\ &+ \frac{c+d}{4} [p_1^{(0)}(x)q_2^{(0)}(y) + q_1^{(0)}(x)p_2^{(0)}(y)] \end{aligned}$$

where

$$r^{(0)}(xy) = \frac{1}{2} \cdot [p^{(0)}(xy) + q^{(0)}(xy)] \quad \text{as in (14).}$$

The formulae (16) and (16') constitute our main result. Having obtained them we may easily "solve" the recurrence relation (16). This is, mathematically, exactly the same problem as in the "ordinary" case since the recurrence equation has exactly the same form. We thus find with

$$(17) \quad \frac{c+d}{2} = k$$

the result

$$(18) \quad r^{(n)}(xy) = (1 - k)^{n-1} r^{(1)}(xy) + [1 - (1 - k)^{n-1}] r_1^{(0)}(x) r_2^{(0)}(y)$$

where $r^{(1)}(xy)$ must be computed from (16'). Or, in the form:

$$(18') \quad r^{(n)}(xy) = r_1^{(0)}(x) r_2^{(0)}(y) + (1 - k)^{n-1} \cdot [r^{(1)}(xy) - r_1^{(0)}(x) r_2^{(0)}(y)]$$

with (from (16')):

$$r^{(1)}(xy) = (1 - k) r^{(0)}(xy) + \frac{k}{2} [p_1^{(0)}(x) q_2^{(0)}(y) + q_1^{(0)}(x) p_2^{(0)}(y)]$$

Next let us investigate what happens as $n \rightarrow \infty$. We may assume that c is *actually different from* d . Otherwise we have the "ordinary" case where $p^{(n)}(xy) = q^{(n)}(xy)$, and so on. Therefore the trivial case $c = d = 0$, that is *complete linkage* for both sexes may be excluded. (The result in this case is, of course:

$$p^{(n)}(xy) = q^{(n)}(xy) = p^{(0)}(xy) \quad \text{for all } n.)$$

Thus we assume that $k > 0$ and (18) gives the result:

$$(19) \quad \lim_{n \rightarrow \infty} r^{(n)}(xy) = r_1^{(0)}(x) r_2^{(0)}(y).$$

Next consider (10) and use (15) and (19). We find:

$$\begin{aligned} \lim_{n \rightarrow \infty} p^{(n+1)}(xy) &= \frac{1-c}{2} \cdot 2 \lim_{n \rightarrow \infty} r^{(n)}(xy) \\ &\quad + \frac{c}{2} \cdot [p_1^{(1)}(x) q_2^{(1)}(y) + q_1^{(1)}(x) p_2^{(1)}(y)] \\ &= (1-c) r_1^{(0)}(x) r_2^{(0)}(y) + \frac{c}{2} \cdot 2 r_1^{(0)}(x) r_2^{(0)}(y). \end{aligned}$$

Hence *the final simple and useful result*:

$$(20) \quad \lim_{n \rightarrow \infty} p^{(n)}(xy) = \lim_{n \rightarrow \infty} q^{(n)}(xy) = r_1^{(0)}(x) r_2^{(0)}(y)$$

where

$$r_1^{(0)}(x) = \frac{1}{2} \cdot [p_1^{(0)}(x) + q_1^{(0)}(x)], \quad r_2^{(0)}(y) = \frac{1}{2} \cdot [p_2^{(0)}(y) + q_2^{(0)}(y)].$$

As n , the number of distinct generations, increases the two gametic distributions $p^{(n)}(xy)$ and $q^{(n)}(xy)$ will tend towards the same distribution which equals the product $r_1^{(0)}(x) \cdot r_2^{(0)}(y)$ where each of these two factors denotes the arithmetic mean of the respective gene probabilities in the initial generation. This holds in case of random mating if $k = \frac{1}{2}(c+d)$, the arithmetic mean of the two recombination values for females and for males, is different from zero.

2. The case of $m=3$ characters.

In this case the distribution of genotypes may be denoted by

$$(21) \quad w^{(n)}(x_1x_2x_3; y_1y_2y_3)$$

where now, with a view to the general case of any m , x_1, x_2, x_3 is used rather than x, y, z . (This same notation was anticipated in (7), where we called x the total maternal, y the total paternal, heritage.) Here x_1 as well as y_1 stands for any of the r genes a_1, \dots, a_r , while x_2 or y_2 stands for any of the r genes b_1, \dots, b_r and x_3 and y_3 for c_1, \dots, c_r , and x_1, x_2, x_3 denotes the maternal, y_1, y_2, y_3 the paternal heritage. A distribution of genotypes contains, as stated before r^{2m} values of which not more than $r^m(r^m+1)/2$ correspond to different types. This last gives if $m=3: r^3(r^3+1)/2$ and if $r=2$ the two numbers are 64 and 36 respectively; we have, for instance the types (ABC; ABC), (ABC; ABc), \dots (abc; abc). The sum of all the r^6 values in (21) equals one.

In our problem we assume at the beginning two different distributions $w^{(0)}(x_1x_2x_3; y_1y_2y_3)$ for the females and $\omega^{(0)}(x_1x_2x_3; y_1y_2y_3)$ for the males. The corresponding distributions of gametes are $p^{(n)}(x_1x_2x_3)$ and $q^{(n)}(x_1x_2x_3)$ with

$$(22) \quad \sum_{x_1} \sum_{x_2} \sum_{x_3} p^{(n)}(x_1x_2x_3) = 1, \quad \sum_{x_1} \sum_{x_2} \sum_{x_3} q^{(n)}(x_1x_2x_3) = 1, \\ (n = 0, 1, \dots).$$

The linkage distribution contains four values with sum one. $v_0=2l_0$ is the probability that the produced gamete has only maternal genes or only paternal genes, $v_i=2l_i$ is the probability that the i^{th} gene be maternal, the two others paternal, or vice versa ($i=1, 2, 3$). Hence

$$(23) \quad v_0 + v_1 + v_2 + v_3 = 2l_0 + 2l_1 + 2l_2 + 2l_3 = 1.$$

The relation between these values and the three r.v.'s, c_{12}, c_{13}, c_{23} is the following (GEIRINGER 1944, p. 34)

$$(24) \quad c_{ij} = v_i + v_j \quad (i = 1, 2, 3, j = 1, 2, 3, i \neq j), \\ v_i = \frac{1}{2}(c_{ij} + c_{ik} - c_{jk}), \quad (i, j, k = 1, 2, 3, i \neq j, j \neq k, i \neq k), \\ v_0 = \frac{1}{2}(2 - c_{12} - c_{13} - c_{23}).$$

In order to derive our recurrence formula, we need again the "marginal" probabilities of gametes, that is, the probability of a gamete which contains, e.g., with respect to the first and the second character the genes x_1, x_2 , or the probability of a gamete which contains with respect to the first character the gene x_1 :

$$(25) \quad p_{12}^{(n)}(x_1x_2) = \sum_{x_3} p^{(n)}(x_1x_2x_3), \quad p_{13}^{(n)}(x_1x_3) = \sum_{x_2} p^{(n)}(x_1x_2x_3), \dots \\ p_1^{(n)}(x_1) = \sum_{x_2} \sum_{x_3} p^{(n)}(x_1x_2x_3) = \sum_{x_2} p_{12}^{(n)}(x_1x_2) = \sum_{x_3} p_{13}^{(n)}(x_1x_3), \dots$$

with

$$(25') \quad \sum_{x_i} \sum_{x_j} p_{ij}^{(n)}(x_ix_j) = 1, \quad \sum_{x_i} p_i^{(n)}(x_i) = 1.$$

Analogous definitions hold for the $q^{(n)}(x_1x_2x_3)$.

The l.d. for the females may be given by c_{ij} or by $v_i = 2l_i$, that for the males by \bar{c}_{ij} or by $\bar{v}_i = 2\bar{l}_i$. We then derive first the formulae which correspond to (10), using either direct explicit computation as in section 1, or the more general conclusions used in the author's previous papers. A first result is

$$(26) \quad \begin{aligned} p^{(n+1)}(x_1 x_2 x_3) &= l_0 [p^{(n)}(x_1 x_2 x_3) + q^{(n)}(x_1 x_2 x_3)] \\ &+ l_1 [p_1^{(n)}(x_1) q_{23}^{(n)}(x_2 x_3) + q_1^{(n)}(x_1) p_{23}^{(n)}(x_2 x_3)] \\ &+ \cdot + \cdot \quad (n = 0, 1, \dots) \end{aligned}$$

and

$$(26') \quad \begin{aligned} q^{(n+1)}(x_1 x_2 x_3) &= \bar{l}_0 [p^{(n)}(x_1 x_2 x_3) + q^{(n)}(x_1 x_2 x_3)] \\ &+ \bar{l}_1 [p_1^{(n)} q_{23}^{(n)}(x_2 x_3) + q_1^{(n)} p_{23}^{(n)}(x_2 x_3)] \\ &+ \cdot + \cdot \quad (n = 0, 1, \dots) \end{aligned}$$

Next we derive from (26), considering (25)

$$(27) \quad \begin{aligned} p_1^{(n+1)}(x_1) &= l_0 [p_1^{(n)}(x_1) + q_1^{(n)}(x_1)] + l_1 [p_1^{(n)}(x_1) + q_1^{(n)}(x_1)] \\ &+ \cdot + \cdot = \frac{1}{2} [p_1^{(n)}(x_1) + q_1^{(n)}(x_1)] \quad (n = 0, 1, \dots) \end{aligned}$$

and in the same way

$$(27') \quad q_1^{(n+1)} = \frac{1}{2} [p_1^{(n)}(x_1) + q_1^{(n)}(x_1)]$$

consequently

$$\begin{aligned} p_1^{(n)}(x_1) &= q_1^{(n)}(x_1), \quad (n \geq 1) \\ p_1^{(n)}(x_1) &= p_1^{(1)}(x_1) = q_1^{(1)}(x_1) = q_1^{(n)}(x_1) \quad (n \geq 1). \end{aligned}$$

Hence we have

$$(28) \quad \begin{aligned} p_1^{(n)}(x_1) &= p_1^{(1)}(x_1) = \frac{1}{2} [p_1^{(0)}(x_1) + q_1^{(0)}(x_1)] \\ q_1^{(n)}(x_1) &= q_1^{(1)}(x_1) = \frac{1}{2} [p_1^{(0)}(x_1) + q_1^{(0)}(x_1)] \quad (n \geq 1). \end{aligned}$$

Hence (26) takes the definite form corresponding to (10'): ($n \geq 1$)

$$(29) \quad \begin{aligned} p^{(n+1)}(x_1 x_2 x_3) &= l_0 [p^{(n)}(x_1 x_2 x_3) + q^{(n)}(x_1 x_2 x_3)] \\ &+ l_1 [p_1^{(1)}(x_1) (q_{23}^{(n)}(x_2 x_3) + p_{23}^{(n)}(x_2 x_3)) + \cdot + \cdot \end{aligned}$$

and in an obvious notation

$$(29') \quad \begin{aligned} q_{123}^{(n+1)} &= \bar{l}_0 [p_{123}^{(n)} + q_{123}^{(n)}] + \bar{l}_1 [p_1^{(1)} (q_{23}^{(n)} + p_{23}^{(n)})] \\ &+ \bar{l}_2 [p_2^{(1)} (q_{13}^{(n)} + p_{13}^{(n)})] + \bar{l}_3 [p_3^{(1)} (q_{12}^{(n)} + p_{12}^{(n)})]. \end{aligned}$$

Now we introduce again the distribution

$$(30) \quad r^{(n)}(x_1 x_2 x_3) = \frac{1}{2} [p^{(n)}(x_1 x_2 x_3) + q^{(n)}(x_1 x_2 x_3)]$$

for which

$$\begin{aligned} r_1^{(n)}(x_1) &= \frac{1}{2} [p_1^{(n)}(x_1) + q_1^{(n)}(x_1)] = \frac{1}{2} [p_1^{(1)}(x_1) + q_1^{(1)}(x_1)] = r_1^{(1)} \\ &= p_1^{(1)} = q_1^{(1)} = \frac{1}{2} [p_1^{(0)} + q_1^{(0)}] = r_1^{(0)}(x_1). \end{aligned}$$

Hence

$$(30') \quad r_i^{(n)}(x_i) = p_i^{(1)}(x_i) = q_i^{(1)}(x_i) = r_i^{(1)}(x_i) = r_i^{(0)}(x_i).$$

Addition of (29) and (29') and multiplication by 1/2 gives the final form of the recurrence formula

$$(31) \quad \begin{aligned} r_{123}^{(n+1)} &= (l_0 + \bar{l}_0)r_{123}^{(n)} + (l_1 + \bar{l}_1)r_{11}^{(0)}r_{23}^{(n)} \\ &+ (l_2 + \bar{l}_2)r_2^{(0)}r_{13}^{(n)} + (l_3 + \bar{l}_3)r_3^{(0)}r_{12}^{(n)} \quad (n = 1, 2, \dots). \end{aligned}$$

Since this hold from $n=1$ on only it has to be complemented by the formula following from (26) and (26') for $n=0$:

$$(31') \quad \begin{aligned} r_{123}^{(1)} &= (l_0 + \bar{l}_0)r_{123}^{(0)} + (l_1 + \bar{l}_1) \cdot \frac{1}{2} [p_1^{(0)}q_{23}^{(0)} + q_1^{(0)}p_{23}^{(0)}] \\ &+ (l_2 + \bar{l}_2) \cdot \frac{1}{2} [p_2^{(0)}q_{13}^{(0)} + q_2^{(0)}p_{13}^{(0)}] \\ &+ (l_3 + \bar{l}_3) \cdot \frac{1}{2} [p_3^{(0)}q_{12}^{(0)} + q_3^{(0)}p_{12}^{(0)}]. \end{aligned}$$

Therefore a statement completely analogous to that at the end of section 1 holds true: *The formula (31) is exactly the same as the "ordinary" formula except that 1) $r^{(n)}(x_1x_2x_3) = \frac{1}{2}[P^{(n)}(x_1x_2x_3) + Q^{(n)}(x_1x_2x_3)]$ takes the place of $P^{(n)}(x_1x_2x_3)$. 2) $l_i + \bar{l}_i = \frac{1}{2}(v_i + \bar{v}_i)$ takes the place of v_i , ($i=0, \dots, 3$), or: $k_{ij} = \frac{1}{2}(c_{ij} + \bar{c}_{ij})$ takes the place of c_{ij} . 3) The recurrence holds from $n=1$ on only. Consequently (31') has to be considered too.*

We may now "solve" (31') in the same way as in the "ordinary" case. Put

$$(32) \quad \begin{aligned} l_i + \bar{l}_i &= \frac{1}{2}(v_i + \bar{v}_i) = s_i, \quad (i = 0, \dots, 3), \quad \sum_1^{0 \dots 3} s_i = 1, \\ \frac{1}{2}(c_{ij} + \bar{c}_{ij}) &= k_{ij}, \quad (i, j = 1, 2, 3; i \neq j). \end{aligned}$$

The solution of (31) is, with the notation used before, for $n \geq 1$:

$$(33) \quad \begin{aligned} r_{123}^{(n)} &= r_1^{(0)}r_2^{(0)}r_3^{(0)} + [(s_0 + s_1)^{n-1} - s_0^{n-1}] \cdot [r_1^{(0)}r_{23}^{(1)} - r_1^{(0)}r_2^{(0)}r_3^{(0)}] \\ &+ [(s_0 + s_2)^{n-1} - s_0^{n-1}] \cdot [r_2^{(0)}r_{13}^{(1)} - r_1^{(0)}r_2^{(0)}r_3^{(0)}] + [\cdot] [\cdot] \end{aligned}$$

or, in terms of the r.v.'s writing

$$(34) \quad m_{ij} = 1 - k_{ij}, \quad s_0 = 1 - \frac{1}{2}(k_{12} + k_{13} + k_{23})$$

we find for $n=1, 2, \dots$

$$(35) \quad r_{123}^{(n)} = r_1^{(0)}r_2^{(0)}r_3^{(0)} + (m_{23}^{n-1} - s_0^{n-1})(r_1^{(0)}r_{23}^{(1)} - r_1^{(0)}r_2^{(0)}r_3^{(0)}) + \dots$$

We still need $r_{12}^{(1)}, r_{13}^{(1)}, r_{23}^{(1)}$ which we obtain from (31')

$$(36) \quad \begin{aligned} r_{ij}^{(1)} &= (s_i + s_j) \cdot \frac{1}{2} \cdot (p_i^{(0)}q_j^{(0)} + q_i^{(0)}p_j^{(0)}) + (1 - s_i - s_j)r_{ij}^{(0)} \\ &= r_{ij}^{(0)} + \frac{1}{2}(s_i + s_j) \cdot [(p_i^{(0)}q_j^{(0)} - p_{ij}^{(0)}) + (q_i^{(0)}p_j^{(0)} - q_{ij}^{(0)})]. \end{aligned}$$

Finally we investigate the limit behavior of $r_{123}^{(n)}, p_{123}^{(n)}, q_{123}^{(n)}$. Assume that all $k_{ij} \neq 0$. It follows immediately from (35) that

$$(37) \quad \lim_{n \rightarrow \infty} r_{123}^{(n)} = r_1^{(0)}r_2^{(0)}r_3^{(0)}.$$

Next we consider (26) and find, using results for $m=2$:

$$\begin{aligned} \lim_{n \rightarrow \infty} p_{123}^{(n+1)} &= v_0 r_1^{(0)} r_2^{(0)} r_3^{(0)} + \frac{v_1}{2} [p_1^{(1)} r_2^{(0)} r_3^{(0)} + q_1^{(1)} r_2^{(0)} r_3^{(0)}] + \cdot + \cdot \\ &= v_0 r_1^{(0)} r_2^{(0)} r_3^{(0)} + \frac{v_1}{2} \cdot 2 r_1^{(0)} r_2^{(0)} r_3^{(0)} + \cdot + \cdot \\ &= r_1^{(0)} r_2^{(0)} r_3^{(0)}. \end{aligned}$$

Hence, as expected: *If all $k_{ij} > 0$:*

$$(38) \quad \lim_{n \rightarrow \infty} p_{123}^{(n)} = \lim_{n \rightarrow \infty} q_{123}^{(n)} = \lim_{n \rightarrow \infty} r_{123}^{(n)} = r_1^{(0)} r_2^{(0)} r_3^{(0)}.$$

If one k_{ij} vanishes, for example $k_{12} = 0$, then the corresponding $m_{12} = 1 - k_{12} = 1$, and $s_1 = s_2 = 0$. It then follows that

$$p_{12}^{(n)} = p_{12}^{(0)}, \quad q_{12}^{(n)} = q_{12}^{(0)}, \quad r_{12}^{(n)} = r_{12}^{(0)}$$

and

$$(38') \quad \lim_{n \rightarrow \infty} p_{123}^{(n)} = \lim_{n \rightarrow \infty} q_{123}^{(n)} = \lim_{n \rightarrow \infty} r_{123}^{(n)} = r_{12}^{(0)} r_3^{(0)}.$$

The case where *all $k_{ij} = 0$* is the ordinary case of complete linkage with, $p_{123}^{(n)} = p_{123}^{(0)}$. If two k_{ij} vanish it follows that the third must vanish.

It can be seen easily that these very elegant results holding if $m=2$ or $m=3$ can not hold in the same way if $m \geq 4$.

3. The general case of $m \geq 4$ characters.

If $m \geq 4$, linkage cannot be completely described in terms of the $m(m-1)/2$ r.v.'s. We need a linkage distribution which may be introduced as follows. GEIRINGER 1944, p. 32). Denote by S the m numbers 1, 2, \dots , m , by A any "subset" of S (including S), by A' the complementary set $A' = S - A$ (for example $A = 1, 3, 4$, $A' = 2, 5, 6, \dots, m$). Then l_A is the probability that a gamete transmitted by a parent contains maternal genes with respect to the characters whose numbers are in A and paternal ones with respect to the other characters, and $l_A = l_{A'}$. If we want to specify we write, for example, for $m=6$, $l_{135} = l_{246}$ and $l_{135} + l_{246} = v_{135}$ which is the probability that the gamete receives with respect to the first, third, and fifth character the maternal, and with respect to the second, fourth and sixth the paternal, gene, or vice versa. There are obviously 2^m such l -values which are equal to each other in pairs and have the sum one, hence there are $M = 2^{m-1} - 1$ independent values. Thus, for $m \geq 4$, $M > m(m-1)/2$ and we see that the complete linkage situation can not be described in terms of the r.v.'s alone (at least not without an additional hypothesis.)

It is a noteworthy result that, in the ordinary case, the recurrence relations have still a very simple and clear structure, if we introduce in analogy to (25) the "marginal" distributions for μ genes where $1 \leq \mu \leq m-1$. The general recurrence formula as derived by GEIRINGER (1944, page 39) may be written in a very condensed form as follows

$$(39) \quad p_s^{(n+1)} = \sum_{(A)} p_A^{(n)} p_{A'}^{(n)} \cdot l_A.$$

This gives, for example for $m=4$, if we use $l_A + l_{A'} = v_A = v_{A'}$.

$$(40) \quad \begin{aligned} p_{1234}^{(n+1)} &= v_0 p_{1234}^{(n)} + [v_1 p_1^{(0)} p_{234}^{(n)} + v_2 p_2^{(0)} p_{134}^{(n)} \\ &+ v_3 p_3^{(0)} p_{124}^{(n)} + v_4 p_4^{(0)} p_{123}^{(n)}] \\ &+ [v_{12} p_{12}^{(n)} p_{34}^{(n)} + v_{13} p_{13}^{(n)} p_{24}^{(n)} + v_{14} p_{14}^{(n)} p_{23}^{(n)}]. \end{aligned}$$

In writing (40) we have already used that $p_i^{(n)} = p_i^{(0)}$.

Now assume again the general situation where l_A and \bar{l}_A denote the respective l.d.'s for females and males, while $p^{(n)}(x) \equiv p^{(n)}(x_1 x_2 \dots x_m) = p_{12}^{(n)} \dots p_m$ and $q^{(n)}(x) \equiv q^{(n)}(x_1 x_2 \dots x_m) = q_{12}^{(n)} \dots p_m$ are the gametic distributions for females and males respectively. In a way analogous to that before we derive for $m=4$

$$(41) \quad \begin{aligned} p_{1234}^{(n+1)} &= l_0 [p_{1234}^{(n)} + q_{1234}^{(n)}] \\ &+ \{ l_1 [p_1^{(1)} q_{234}^{(n)} + q_1^{(1)} p_{234}^{(n)}] + \cdot + \cdot + \cdot \} \\ &+ \{ l_{12} [p_{12}^{(n)} q_{34}^{(n)} + q_{12}^{(n)} p_{34}^{(n)}] + \cdot + \cdot \} \\ q_{1234}^{(n+1)} &= \bar{l}_0 [p_{1234}^{(n)} + q_{1234}^{(n)}] \\ &+ \{ \bar{l}_1 [p_1^{(1)} q_{234}^{(n)} + q_1^{(1)} p_{234}^{(n)}] + \cdot + \cdot + \cdot \} \\ &+ \{ \bar{l}_{12} [p_{12}^{(n)} q_{34}^{(n)} + q_{12}^{(n)} p_{34}^{(n)}] + \cdot + \cdot \} \end{aligned}$$

and introduce again

$$(42) \quad r_{1234}^{(n)} = \frac{1}{2} [p_{1234}^{(n)} + q_{1234}^{(n)}]$$

and find

$$(43) \quad p_i^{(1)} = q_i^{(1)} = r_i^{(1)} = \frac{1}{2} \cdot (p_i^{(0)} + q_i^{(0)}) = r_i^{(0)} \quad (i = 1, \dots, m).$$

If we now add the two formulae (41) and introduce $r^{(n)}$ we clearly see that the terms with $(l_i + \bar{l}_i)$ ($i=0, \dots, 4$) will, as before, depend on the r -distribution alone while the last three terms with factors $(l_{ij} + \bar{l}_{ij})$ cannot be expressed in terms of the r -distribution alone. We obtain, using (42) and (43)

$$(45) \quad \begin{aligned} p_{1234}^{(n+1)} &= v_0 r_{1234}^{(n)} + \{ v_1 r_1^{(0)} r_{234}^{(n)} + \cdot + \cdot + v_4 r_4^{(0)} r_{123}^{(n)} \} \\ &+ \{ l_{12} [p_{12}^{(n)} q_{34}^{(n)} + q_{12}^{(n)} p_{34}^{(n)}] + \cdot + \cdot \} \\ q_{1234}^{(n+1)} &= \bar{v}_0 r_{1234}^{(n)} + \{ \bar{v}_1 r_1^{(0)} r_{234}^{(n)} + \cdot + \cdot + \bar{v}_4 r_4^{(0)} r_{123}^{(n)} \} \\ &+ \{ \bar{l}_{12} [p_{12}^{(n)} q_{34}^{(n)} + q_{12}^{(n)} p_{34}^{(n)}] + \cdot + \cdot \} \end{aligned}$$

and upon addition and division by two:

$$(46) \quad \begin{aligned} r_{1234}^{(n+1)} &= (l_0 + \bar{l}_0) r_{1234}^{(n)} + \{ (l_1 + \bar{l}_1) r_1^{(0)} r_{234}^{(n)} + \cdot + \cdot + \cdot \} \\ &+ \{ (l_{12} + \bar{l}_{12}) \cdot \frac{1}{2} \cdot [p_{12}^{(n)} q_{34}^{(n)} + q_{12}^{(n)} p_{34}^{(n)}] + \cdot + \cdot \}. \end{aligned}$$

If we consider a greater value of m there are, if $m=2\mu$ or $2\mu+1$ respectively $(\mu+1)$ groups of terms, and of these $\mu+1$ groups the first two groups only can be expressed in terms of the r -distribution while all other $(\mu+1) - 2$

$= \mu - 1$ groups will contain the $p_A^{(n)}$ and $q_A^{(n)}$. Hence the elegant results found for $m=2$ and $m=3$ no longer hold in full simplicity. The mean of the two l.d.'s is still the l.d. in the recurrence relations but the gametic distributions appear both and not their mean only.

Formula (46) is typical. We can easily get the analogous result for any m , for instance for $m=7$ (of course with other l-values):

$$(47) \quad \begin{aligned} r_{123\dots 67}^{(n+1)} &= (l_0 + \bar{l}_0)r^{(n)}_{123\dots 67} + \{ (l_1 + \bar{l}_1)r_1^{(0)}r^{(n)}_{23\dots 67} + \dots (7 \text{ terms}) \} \\ &+ \{ (l_{12} + \bar{l}_{12}) \cdot \frac{1}{2} \cdot [p_{12}^{(n)}q_{34\dots 7}^{(n)} + q_{12}^{(n)}p_{34\dots 7}^{(n)}] + \dots (21 \text{ terms}) \} \\ &+ \{ (l_{123} + \bar{l}_{123}) \cdot \frac{1}{2} \cdot [p_{123}^{(n)}q_{4567}^{(n)} + q_{123}^{(n)}p_{4567}^{(n)}] + \dots (35 \text{ terms}) \} \end{aligned}$$

Now it is interesting to see that notwithstanding this less simple structure of the recurrence relations the *limit theorem is still the same*. We shall derive it directly from the recurrence formula without using an explicit "solution." We shall use induction. Consider (46) and assume that all six mean r.v.'s, $k_{ij} = (c_{ij} + \bar{c}_{ij}) \frac{1}{2}$ are greater than zero, that means, for no (i, j) both c_{ij} and \bar{c}_{ij} vanish. Write

$$(46') \quad \begin{aligned} r_{1234}^{(n+1)} - (l_0 + \bar{l}_0)r_{1234}^{(n)} &= \{ (l_1 + \bar{l}_1)r_1^{(0)}r_{234}^{(n)} + \dots + \dots \} \\ &+ \{ (l_{12} + \bar{l}_{12}) \cdot \frac{1}{2} [p_{12}^{(n)}q_{34}^{(n)} + q_{12}^{(n)}p_{34}^{(n)}] + \dots + \dots \}. \end{aligned}$$

The right side of this equation contains merely distributions of orders 1, 2, and 3. For such distributions we studied the limit behavior before. Consider for example $r_{234}^{(n)}$. Since k_{23}, k_{24}, k_{34} are $\neq 0$ we know from section 2 that $r_{234}^{(n)} \rightarrow r_2^{(0)}r_3^{(0)}r_4^{(0)}$, hence $r_1^{(0)}r_{234}^{(n)} \rightarrow r_1^{(0)}r_2^{(0)}r_3^{(0)}r_4^{(0)}$ and the same holds for $r_2^{(0)}r_{134}^{(n)} \rightarrow r_1^{(0)}r_2^{(0)}r_3^{(0)}r_4^{(0)}$. Next consider $p_{12}^{(n)}$, because of $k_{12} \neq 0$ and our result for $m=2$, $p_{12}^{(n)} \rightarrow r_1^{(0)}r_2^{(0)}$ and $q_{34}^{(n)} \rightarrow r_3^{(0)}r_4^{(0)}$ since $k_{34} \neq 0$. Furthermore

$$\begin{aligned} (l_1 + \dots + l_4) + (l_{12} + l_{13} + l_{14}) + (\bar{l}_1 + \dots + \bar{l}_4) + (\bar{l}_{12} + \bar{l}_{13} + \bar{l}_{14}) \\ = \frac{1}{2} - l_0 + \frac{1}{2} - \bar{l}_0 = 1 - (l_0 + \bar{l}_0). \end{aligned}$$

Hence the right side of (46) converges towards

$$[1 - (l_0 + \bar{l}_0)]r_1^{(0)}r_2^{(0)}r_3^{(0)}r_4^{(0)}.$$

The left side of (46') is of the form $x_{n+1} - \alpha x_n$ and the whole equation is of the form $x_{n+1} - \alpha x_n = y_n$ where $\lim_{n \rightarrow \infty} y_n = y = [1 - (l_0 + \bar{l}_0)]r_1^{(0)} \dots r_4^{(0)}$. It is an easily proved theorem of analysis that for an equation of this form if $|\alpha| < 1$, and $\lim_{n \rightarrow \infty} y_n = y$ then $\lim_{n \rightarrow \infty} x_n = y/1 - \alpha$. Now here $\alpha = l_0 + \bar{l}_0$ and this is less than one unless all r.v.'s are zero. Hence $\lim_{n \rightarrow \infty} x_n = y/1 - l_0 - \bar{l}_0$ and consequently

$$(48) \quad \lim_{n \rightarrow \infty} r_{1234}^{(n)} = r_1^{(0)}r_2^{(0)}r_3^{(0)}r_4^{(0)}.$$

Next consider the first formula (45). We find, using (48) and our results for $m=2$, and $m=3$:

$$\lim_{n \rightarrow \infty} p_{1234}^{(n)} = v_0 r_1^{(0)}r_2^{(0)}r_3^{(0)}r_4^{(0)} + v_1 r_1^{(0)} \dots r_4^{(0)} + \dots + \dots$$

$$\begin{aligned}
 &+ 2!_{12}r_1^{(0)} \dots r_4^{(0)} + \dots \\
 &= r_1^{(0)} \dots r_4^{(0)} \cdot [v_0 + v_1 + \dots + v_4 + v_{12} + v_{13} + v_{14}] \\
 &= r_1^{(0)}r_2^{(0)}r_3^{(0)}r_4^{(0)}.
 \end{aligned}$$

Hence, just as before: *If all $k_{ij} \neq 0$*

$$(49) \quad \lim_{n \rightarrow \infty} p_{1234}^{(n)} = \lim_{n \rightarrow \infty} q_{1234}^{(n)} = r_1^{(0)}r_2^{(0)}r_3^{(0)}r_4^{(0)}.$$

In the same way, using (48), (49), and the results for $m < 4$ we prove for $m = 5$ the result, which corresponds to (49), and so we go on. Our final result is that, for any m if $k_{ij} = \frac{1}{2}(c_{ij} + \bar{c}_{ij}) > 0$:

$$(50) \quad \lim_{n \rightarrow \infty} p_{12 \dots m}^{(n)} = \lim_{n \rightarrow \infty} q_{12 \dots m}^{(n)} = r_1^{(0)}r_2^{(0)} \dots r_m^{(0)}$$

where, as before,

$$(50') \quad r_i^{(0)} = \frac{1}{2}(p_i^{(0)} + q_i^{(0)}), \quad (i = 1, 2 \dots m)$$

with

$$\begin{aligned}
 p_i^{(0)} &\equiv p_i^{(0)}(x_i) \\
 &= \sum_{x_1} \dots \sum_{x_{i-1}} \sum_{x_{i+1}} \dots \sum_{x_m} p^{(0)}(x_1 \dots x_{i-1} x_i x_{i+1} \dots x_m), \\
 (50'') \quad q_i^{(0)} &\equiv q_i^{(0)}(x) \\
 &= \sum_{x_1} \dots \sum_{x_{i-1}} \sum_{x_{i+1}} \dots \sum_{x_m} q^{(0)}(x_1 \dots x_{i-1} x_i x_{i+1} \dots x_m).
 \end{aligned}$$

In words: Consider with respect to m genotypes an arbitrary distribution for males and another one for females, assume random mating and not necessarily identical l.d.'s for the two sexes, but such that the $m(m-1)/2$ "mean recombination values" $k_{ij} = \frac{1}{2}(c_{ij} + \bar{c}_{ij})$ are all different from zero. Denote by $p^{(n)}(x_1 \dots x_m)$ and $q^{(n)}(x_1 \dots x_m)$ the distribution of gametes for females and males respectively in the n^{th} generation and by $r^{(0)}(x_1 \dots x_m) = \frac{1}{2}[p^{(0)}(x_1 \dots x_m) + q^{(0)}(x_1 \dots x_m)]$ the mean distribution of gametes for the initial generation with the corresponding mean gene distribution $r_i^{(0)}$ of the i^{th} character. Then, as n increases, both, $p^{(n)}(x)$ and $q^{(n)}(x)$ will tend towards the same limit distribution, where, according to (50), the m genes are independently distributed. Moreover: The gene distribution for each single character remains the same for males and for females and for all n from the first filial generation on:

$$\begin{aligned}
 (51) \quad q_i^{(n)} = p_i^{(n)} = r_i^{(n)} = q_i^{(1)} = p_i^{(1)} = r_i^{(1)} = r_i^{(0)} &= \frac{p_i^{(0)} + q_i^{(0)}}{2}, \\
 &(i = 1, \dots, m).
 \end{aligned}$$

Also because of (50) we have for the distribution of genotypes

$$\begin{aligned}
 (52) \quad \lim_{n \rightarrow \infty} \omega^{(n)}(x_1 \dots x_m; y_1 \dots y_m) \\
 = r_1^{(0)}(x_1) \dots r_m^{(0)}(x_m)r_1^{(0)}(y_1) \dots r_m^{(0)}(y_m).
 \end{aligned}$$

If the k_{ij} are not all different from zero we have within the considered linkage group of size m smaller groups of completely linked genes and results analogous to (38'). If for instance $m=6$ and the values k_{12} , k_{13} , and (consequently) k_{23} vanish while the twelve other values k_{ij} are different from zero the result is

$$\lim_{n \rightarrow \infty} p^{(n)}_{12 \dots 6} = \lim_{n \rightarrow \infty} q^{(n)}_{12 \dots 6} = r_{123}^{(0)} r_4^{(0)} r_5^{(0)} r_6^{(0)}$$

where, corresponding to the complete linkage of the first three characters,

$$p_{123}^{(n)} = q_{123}^{(n)} = p_{123}^{(0)} = q_{123}^{(0)} = r_{123}^{(0)}, \quad (n = 0, 1, \dots).$$

On the whole we see that the main results concerning random mating of m linked characters are not changed essentially if the linkage values are different for the two sexes. The "mean linkage distribution" $\frac{1}{2}(l_A + \bar{l}_A)$ takes the place of the ordinary l.d. The analogy to the "ordinary" case is complete for $m \leq 3$ characters. If $m \geq 4$ the limit theorem is still the usual type while the recurrence relations present a "mixed" structure.

SUMMARY

On the basis of Mendel's Theory of Heredity the mathematics of random breeding for autosomal factors is worked out under the following assumptions: 1) Any number, finite or infinite, of distinct, non overlapping generations is considered; 2) the number of alleles and the number of Mendelian factors is arbitrary; 3) the "crossover distributions" for males and females are not necessarily equal.

LITERATURE CITED

- GEIRINGER, HILDA, 1944 On the probability theory of linkage in Mendelian heredity. *Ann. Math. Stat.* **15**: 25-57.
 1945 Further remarks on linkage theory in Mendelian heredity. *Ann. Math. Stat.* **16**: 390-393.
- JENNINGS, H. S., 1917 The numerical results of diverse systems of breeding, with respect to two pairs of characters, linked or independent, with special relation to the effect of linkage. *Genetics* **2**: 97-154.
 1923 The numerical relations in the crossing over of the genes, with a critical examination of the theory that the genes are arranged in a linear series. *Genetics* **8**: 393-457.
- ROBBINS, R. B., 1918a Applications of mathematics to breeding problems. II. *Genetics* **3**: 73-92.
 1918b Some applications of mathematics to breeding problems. III. *Genetics* **3**: 375-389.

GENETICALLY REDUCED PROLIFICACY IN RATS¹

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A case of inherited partial sterility in rats, characterized by increased uterine embryonic resorptions and a corresponding decrease in average number of young born, has been described by WALETZKY and OWEN (1942). The genetically reduced prolificacy in these rats is of particular interest because it occurs in both sexes. This paper presents the results of five generations of tests of these partially sterile rats when mated *inter se* and with non-sterile controls.

REVIEW OF LITERATURE

Embryonic resorptions have been reported for most domestic and laboratory animals, by HAMMOND (1921), JONES (1922), EVANS and BISHOP (1923), LONG and PARKES (1924), MACDOWELL (1924), IBSEN (1928), GREGORY (1932), HINMAN (1933), ALLEN and MACDOWELL (1940), HAMILTON (1941). The estimates of average resorption rates,

$$\frac{\text{resorbing embryos}}{\text{total placental sites}},$$

in different species vary from .01 to .39, while estimates of average total egg loss,

$$1 - \frac{\text{normal placental sites}}{\text{total corpora lutea}},$$

vary from .07 to .37. These total mortality figures agree closely with estimates of prenatal mortality computed from corpora lutea counts and young born.

Specific sources of variation in total prenatal mortality have been demonstrated by altering the environment or genetic constitution of the breeding stock. HAMMOND (1941) has reviewed the literature on the more important genetic and environmental factors that affect the reproductive processes of fertilization, implantation and embryonic resorption.

KIRKHAM (1917, 1919) working with yellow mice demonstrated that embryonic mortality could be caused by inherited lethals. Other cases of embryonic death due to recessive zygotic lethals are rather common.

In one strain of rabbits HAMMOND (1934) found low litter size to be associated with a high rate of fetal atrophy (.45 of total implantations). This was inherited as a recessive maternal character. Homozygous does produced the same percentage of atrophic fetuses whether mated with bucks of the same

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strain or with bucks of an unrelated strain. Reciprocal crosses between strain H (.45 atrophy) and strain F (.13 atrophy) produced an F_1 with .15 fetal atrophy. Backcrosses to the parental strains gave rabbits which showed an average of .33 and .14 fetal atrophy, respectively.

BURACK and co-workers (1939) compared 400 pregnancies of female rats of the Albany strain in which fertility was low with 140 control pregnancies from a strain of rats of relatively high fertility. The litter sizes were 5.4 and 8.7, respectively. Studies of the uteri from rats of the partially sterile strain showed a high rate (.25) of spontaneous fetal resorption. There was marked variation in this strain in number of resorbing sites, time of onset of the resorption and the rate of resorption. The control strain, on the other hand, had a low incidence (.027) of resorption.

SNELL (1933, 1935) showed that when X-rayed male mice were mated before the onset of complete sterility to untreated females, approximately 33 percent of the offspring produced litters of small size. Data were obtained from one of these partially sterile individuals and his descendants for a study of the type of inheritance and embryological basis of the trait. The average size of seven litters by this male was 3.7, as compared to the average of 8 for the entire colony. Additional matings between this male and normal females resulted in the formation of the usual number of zygotes, but approximately .42 of these were non-viable as compared to .20 of 110 embryos of control stock. Twenty-seven offspring from matings of semi-sterile males to normal females were tested and placed into two classes on the basis of litter size. The first was a group of 13 with the size of litters ranging from 3.5 to 5.3—semi-sterile; the second a group of 14 with the litter size ranging from 6.5 to 10.5—normal. Thus crosses between semi-sterile and normal mice resulted in the production of semi-sterile, normal and non-viable in the ratio of 2:2:3. SNELL concluded that the results were best explained by supposing the semi-sterile mice to be heterozygous for a translocation.

KOLLER and AUERBACH (1941) and HERTWIG (1935, 1938, 1940) have developed lines of semi-sterile mice, each from a different male treated by the X-ray technique of SNELL. KOLLER (1944) reported a relatively high degree of association between actual breeding tests and fertility estimated from the results of a cytological analysis of the testes of individuals in each of three "interchange" lines of mice. Litter size of control and experimental animals were used to obtain a coefficient of fertility. He found that the fertility of the three lines was 39 percent of the controls in line A, 45.7 percent in line B and 46.5 percent in line T, when fertile matings only were included in computing average litter size.

SNELL (1946) has summarized the experimental results from experiments in which translocations have been induced in mice by irradiation.

The partially sterile condition in rats reported by WALETZKY and OWEN (1942) occurred spontaneously in a single male. Half of the 16 tested F_1 and F_2 males and females from this male were partially sterile and half were normal. Matings of partially sterile and normal individuals resulted in a normal number of implantation sites but approximately 60 percent of these sites under-

went resorption. At the earliest stage examined, eight to nine days, approximately half of the sites contained normal embryos, the other half, solid placentomata. The hypothesis they formulated to explain these results was a heterozygous reciprocal translocation. BOURICIUS (1948) has studied the embryonic development of normal and abnormal embryos in the uteri of female rats in partially sterile \times normal matings.

EXPERIMENTAL PROCEDURE AND RESULTS

A partially sterile male and four of his sons were procured from DR. WALETZKY as the foundation stock for this study. The normal tester males and females were obtained from a colony of albino rats unrelated to the partially sterile rats as far as ancestry could be traced. Most of the tester females had had their fourth litter and hence had a known fertility history. The males, on the other hand, were virgins, and before being used as normal testers were mated to normal females to estimate their prolificacy.

Tester Stock

In order to estimate the embryonic resorption rate in the control stock, 118 females were mated to 61 males and killed between the 13th day and the end of gestation. The reproductive organs were exposed; the number of corpora lutea, the number and position in the uterus of normal (no visible signs of death or resorption) and resorbing sites in each uterine horn, the diameter of uterine contents at each normal and resorbing site and the average intrauterine crown-rump length of the normal fetuses were recorded.

Ninety-four (8.5 percent) embryonic resorptions were found among the 1107 sites in the exposed uteri of the 118 tester females which were mated to tester males (table 1). These resorbing sites were found in 62 (52.5 percent) of the females. The number of resorptions per female varied from one to four, while the range in percentage of resorptions per female was from 7 percent to 50 percent. The resorptions were randomly distributed between the two horns, and within horns there was no tendency for resorptions to be adjacent (table 2). The differences in resorption rates between groups of females of different parity were statistically significant. They were due to the higher percentage of resorptions in females that had dropped more than two litters. The percentage of resorptions did not increase significantly in the latter part of gestation (table 3). Hence it appears that death followed by resorption generally occurs before the 10 mm crown-rump stage.

The mean number of corpora lutea and normal embryos in the 118 tester females was 10.9 and 8.6, respectively (table 1). On the assumption that each corpus luteum represents the ovulation of a single ovum, the mean difference of 2.3 indicates an average egg mortality of 21 percent between the time of ovulation and the last third of the gestation period (7 percent resorption plus 14 percent non-implanted ovulated eggs). The differences between average egg mortality rates were significantly and positively correlated with the parity of the females (table 1). Although there is no definite trend for litters in the latter stages of pregnancy to contribute more to the total egg mortality than

TABLE 1

The number of corpora lutea (CL) in the ovaries, the number of normal (N) and resorbing (R) sites in the uteri, the percentages of resorptions, the number of non-implanted ovulated eggs (P) and the percentage mortality of P and P+R in 118 tester females mated to tester males and grouped according to side of occurrence and parity number of the female.

SIDE OF OCCURRENCE	PARITY NUMBER	NO. OF TESTER FEMALES	CL	N	R	N+R	R AS % OF N+R	P	P AS % OF CL	P+R AS % OF CL
Right	1	40	197	165	13	178	6.6	19	9.6	16.2
	2	22	124	107	5	112	4.0	12	9.7	13.7
	3	22	103	85	4	89	3.9	14	13.6	17.5
	4	11	63	51	5	56	8.9	7	11.1	19.0
	5 or more	23	127	95	12	107	11.2	20	15.7	25.2
Left	1	40	210	172	9	181	5.0	29	13.8	18.1
	2	22	121	91	6	97	6.2	24	19.8	24.8
	3	22	135	100	18	118	15.3	17	12.6	25.9
	4	11	55	38	3	41	7.3	14	25.5	30.9
	5 or more	23	153	109	19	128	14.8	25	16.3	28.8
Combined	1	40	407	337	22	359	6.1	48	11.8	17.2
	2	22	245	198	11	209	5.3	36	14.7	19.2
	3	22	238	185	22	207	10.6	31	13.0	22.3
	4	11	118	89	8	97	8.2	21	17.8	24.6
	5 or more	23	280	204	31	235	13.2	45	16.1	27.1
Total		118	1288	1013	94	1107		181		
Av. per female			10.9	8.6	.8	9.4	8.5	1.5	14.1	21.4

do those from earlier stages, there is a significant difference in this mortality at the various fetal stages (table 3). Most of this difference arises in the low mortality of the 11-15 mm and the high mortality of the 33 mm crown-rump stages.

Tester × Partially Sterile Matings

Tester females were mated to the five foundation males and were laparotomized between the 12th and 16th day of gestation to determine the presence of normal and resorbing embryos. Vaginal smears were taken daily until the placental sign was observed or until pregnancy could be detected by abdominal palpation. Males were classified as partially sterile if they sired a significantly greater proportion of resorbing embryos than expected on the basis of resorption rate in the tester stock.

The F_1 progeny (males and females) of the partially sterile male × tester female matings were backcrossed with normal testers, and the females of these matings were laparotomized between the 12th and 16th day of gestation. The number of corpora lutea, number and position of normal and resorbing sites,

TABLE 2

Distribution of the resorbing sites between right and left uterine horns and the frequency of adjacent resorbing sites in tester females mated to tester males.

NUMBER OF RESORPTIONS	HORN		FREQUENCY	TOTAL RESORBING SITES	CASES OF ADJACENT RESORBING SITES
	RIGHT	LEFT			
1	1	0	19	19	—
	0	1	19	19	—
2	2	0	3	6	2
	1	1	7	14	—
	0	2	7	14	3
3	3	0	0	0	—
	2	1	2	6	1
	1	2	3	9	2
	0	3	1	3	1
4	0	4	1	4	1

and the average diameter of uterine horn and contents of each site were recorded for each female. These F_1 individuals were then classified either normal or partially sterile, depending on the proportion of resorbing embryos.

A summary of the results obtained in matings of the four sons of the original semi-sterile male to tester females is given in table 4. Each of these males sired more than the requisite proportion of resorptions (more than 25 percent of the uterine sites of their mates resorbing) and were classified as partially sterile.

TABLE 3

The number of corpora lutea (CL), of normal (N) and resorbing (R) sites, the percent of resorbing sites, the number of non-implanted ovulated eggs (P) and the percentage mortality of P and P+R for 77 tester females grouped according to crown-rump length of normal embryos.

CROWN RUMP LENGTH	NO. OF TESTER FEMALES	CL	N	R	N+R	R AS % OF N+R	P	P AS % OF CL	P+R AS % OF CL
8-10 mm.	8	92	71	7	78	9.0	14	15.2	22.8
11-15	21	226	192	8	200	4.0	26	11.5	15.0
16-20	24	252	191	22	213	10.3	39	15.5	24.2
21-25	13	148	110	9	119	7.6	29	19.6	25.7
26-32	7	72	57	6	63	9.5	9	12.5	20.8
33-Over	4	48	31	5	36	13.9	12	25.0	35.4
Total	77	838	652	57	709		129		
Av. per female		10.9	8.5	.7	9.2	8.0	1.7	15.4	22.2

Furthermore, the average total egg loss in the mates was 60.8 percent as compared with 21.4 percent in the normal tester matings. Stated in terms of ova that resulted in normal embryos, the percentage figures are 39.2 and 78.5, respectively. This means that of the zygotes sired by partially sterile males, only 50 percent as many as those sired by normal tester males were viable.

TABLE 4

The number of corpora lutea (CL), normal (N) and resorbing sites (R), the percent of resorbing sites and the number of non-implanted ovulated eggs (P), and the percentage mortality of P and P+R in the mates of four sons of the original partially sterile male

MALE NO.	NO. OF MATES	CL	N	R	N+R	R AS % OF N+R	P	P AS % OF CL	P+R AS % OF CL
92	1	5	1	4	5	80.0	0	—	80.0
98	1	9	4	5	9	55.6	0	—	55.6
112	10	80	33	42	75	56.0	5	6.3	58.8
408	9	82	31	47	78	60.3	4	4.9	62.2
Total	21	176	69	98	167	—	9	—	—
Average		8.4	3.3	4.7	8.0	58.7	0.4	5.1	60.8

The descendants of two of these males (Nos. 112 and 408) were tested for prolificacy and classified into normal and partially sterile groups. The reproductive data for these are presented in table 5.

TABLE 5

Reproductive data for female mates in the matings of partially sterile (PS) and normal (N) offspring of partially sterile rats to tester rats

CLASSIFICATION	NO. OF ANI-MALS	NO. OF MAT-INGS	CL	N	R	N+R	R AS % OF N+R	P	P AS % OF CL	P+R AS % OF CL
PS Males	30	84	802	285	346	631	54.8	171	21.3	64.5
PS Females	33	33	286	76	154	230	67.0	56	19.6	73.4
Total	63	117	1088	361	500	861	58.1	227	20.9	66.8
N Males	38	116	1198	944	75	1019	7.4	179	14.9	21.2
N Females	55	57	584	506	28	534	5.2	50	8.6	13.4
Total	93	173	1782	1450	103	1553	6.6	229	12.9	18.6

Sixty-three (40 percent) of these were classified as partially sterile and 93 (60 percent) as normal rats. The partially sterile group produced 58.1 percent resorbing sites and the average total egg loss was 66.8 percent, while in the rats classified normal the resorption rate was 6.6 percent and the egg loss was 18.6 percent. The fertility (viable embryos) of these partially sterile rats was 42 percent of that of the normal tester females.

Of the 156 individuals tested for partial sterility, 137 were by partially sterile sires and out of tester dams, 17 by tester sires and out of partially sterile dams, while two were the result of mating partially sterile males to partially sterile females.

Measurements of width of resorbing and normal embryos taken through the uterine wall are summarized in table 6. Size differences are apparent as early as the 12th day of gestation. A few resorbing embryos of later stages were observed, but in general these figures further substantiate the observations of WALETZKY and OWEN (1942) in regard to early mortality.

TABLE 6
*Average width of resorbing and normal sites from the
11th to 19th day of gestation*

AGE OF EMBRYOS DAYS	NORMAL			RESORBING		
	NO.	AVERAGE DIAMETER	STANDARD DEVIATION	NO.	AVERAGE DIAMETER	STANDARD DEVIATION
11-12	4	5.75 mm	.96	2	4.0 mm	—
12-13	5	7.5	.35	4	4.4	.3
13-14	6	8.8	.41	14	4.7	1.03
14-15	14	9.8	.67	15	4.2	.49
15-16	16	11.5	.53	19	4.6	1.18
16-17	5	13.2	.36	2	3.3	—
17-18	9	14.6	.84	5	3.8	.57
18-19	8	14.1	.63	17	3.9	.55

The occurrence of early mortality suggests that intra uterine crowding, as measured by total placental sites, would not increase the rate of resorption. In order to check this, the percentage of resorptions were classified by the total number of sites per pregnant female. These rates of resorption are shown in tables 7 and 8 subdivided on the basis of females mated to males classified normal and partially sterile and from females classified normal and partially sterile mated to normal tester males. In both types of matings the total intra-uterine mortality appears to be independent of the total number of fetuses in the horn.

Nine tester females who had conceived to partially sterile males were mated to normal males for their next pregnancy. The results showed no evidence of subsequent litter size being associated with previous resorption which was 70 percent. The average resorption rate in these pregnancies was 10 percent.

Partially Sterile X Partially Sterile Matings

Female rats that were classified partially sterile were mated to partially sterile males and allowed to reach term. In many cases Caesarean sections were made to save the life of the female and her young, and, at the time of operation, the number of corpora lutea and the number and position of the normal and resorbing sites were recorded.

TABLE 7

Percentage of resorbing sites classified by the total number of sites in the horns of female mates of partially sterile and normal males mated to normal tester females

TOTAL SITES IN ONE HORN	HORNS FROM MATES OF MALES CLASSIFIED PARTIALLY STERILE				HORNS FROM MATES OF MALES CLASSIFIED NORMAL			
	FRE-QUENCY	TOTAL N	TOTAL R	R AS % OF N+R	FRE-QUENCY	TOTAL N	TOTAL R	R AS % OF N+R
1	7	2	5	71.4	5	4	1	20
2	20	16	24	60.0	24	45	3	6.3
3	24	34	38	52.8	38	101	13	11.4
4	41	73	91	55.5	26	99	5	4.8
5	34	81	89	52.4	50	230	20	8.0
6	19	49	65	57.1	38	210	18	7.9
7	8	26	30	53.6	9	56	7	11.1
8	1	4	4	50.0	16	122	6	4.7
9					5	42	3	6.7
10					2	20	0	0
11					1	11	0	0
TOTAL	154	285	346	54.8	214	940	76	7.5

TABLE 8

Percentage of resorbing sites classified by the total number of sites in the horns of partially sterile and normal females mated to normal tester males

TOTAL SITES IN ONE HORN	PARTIALLY STERILE FEMALES				NORMAL FEMALES			
	FRE-QUENCY	TOTAL N	TOTAL R	R AS % OF N+R	FRE-QUENCY	TOTAL N	TOTAL R	R AS % OF N+R
1	2	0	2	100	4	4	0	0
2	12	10	14	58.3	4	8	0	0
3	18	16	38	70.4	19	54	3	5.3
4	23	32	60	65.2	27	106	2	1.9
5	6	11	19	63.3	18	87	3	3.3
6	2	3	9	75.0	26	147	9	5.8
7	0				7	45	4	8.2
8	1	3	5	62.5	5	38	2	5.0
9	1	2	7	77.8	1	8	1	11.1
10								
11					1	9	2	18.2
TOTAL	65	77	154	66.7	112	506	26	4.9

Partially sterile individuals mated *inter se* have produced few young. Laparotomies of six females have shown 57 corpora lutea, 9 normal and 38 resorbing sites (81 percent resorptions), which represents a total egg loss of 48,

or 84 percent. Only a small proportion of the viable young reached weaning age because of starvation and maternal cannibalism; a few others have been raised following transfer to foster dams. Of three rats tested, one was classified normal and the other two partially sterile. No case of rats homozygous for the translocation has been discovered.

New Partially Sterile Line

An interesting deviate from the average rate of resorption in the tester rats was one particular male (No. 1255) who was being tested on normal tester mates, prior to use as a tester male. This rat sired 14 normal and 16 resorbing embryos. This condition was also transmitted to his offspring (table 9), and has the same general characteristics as the partial sterility found in WALETZKY'S strain of rats. The litter sizes for the ancestors and collateral relatives of male 1255 were checked. His sire's litters were of normal size, but his dam consistently produced litters of small size, as did his full sister. However, the pedigree analysis did not lead to any definite interpretation of where the partial sterility originated.

TABLE 9

Reproductive data for female mates in the matings of partially sterile and normal offspring of male 1255 to tester rats

CLASSIFICATION OF OFFSPRING	NUMBER	NO. OF MATES	CL	N	R	N+R	R AS % OF CL	P	P AS % OF CL	P+R AS % OF CL
PS Males	3	6	66	33	23	56	41.1	10	15.2	50.0
N Males	2	5	57	49	4	53	7.5	4	7.0	14.0
PS Females	0	—	—	—	—	—	—	—	—	—
N Females	3	3	39	28	1	29	3.4	10	25.6	28.2

DISCUSSION

Partially sterile \times normal matings resulted in the production of approximately 60 percent resorbing placental sites, while in the control matings the resorption rate was 8.5 percent. The results of this experiment indicate that normal and partially sterile individuals are produced with equal frequency in the living offspring of the partially sterile times normal cross. No partially sterile animals were found among the tested offspring of the normal times normal matings, with one exception, No. 1255. Examination of embryos 8-9 days showed that about 50 percent are normal; the other half were mainly solid moles, but undifferentiated embryos were found at some sites. Macroscopic differences between normal and resorbing sites can be detected after the 11th day of gestation, while instances of more mature sites resorbing were extremely rare in these rats. All these observations are in agreement with the early results of WALETZKY and OWEN (1942).

A single recessive or a balanced lethal condition will not account for the observed results because non-viable embryos occur in the F_1 of crosses of par-

tially sterile to normal. If a dominant semi-lethal were assumed, the heterozygotes (Ss) would be either partially sterile or lethals. These combined should equal the frequency of the homozygous normals (ss) in the offspring of matings of partially sterile (Ss) \times normal (ss). In the case under consideration the ratio of partially sterile alone to normal was approximately equal. Hence the ratio of the combined numbers of partially sterile and lethal to normal deviated widely from equality, making the hypothesis of a dominant partial lethal untenable.

On the basis of the breeding results obtained in this study it is felt that the original hypothesis of WALETZKY and OWEN (1942) is the most tenable, viz., that this partially sterile condition in rats is due to a heterozygous reciprocal translocation. Confirmation of this hypothesis must be obtained by cytological examination of the germinal tissue of partially sterile males.

The breeding data obtained by many investigators from different crosses of individuals carrying a reciprocal translocation indicate that the cytological behavior of segmental interchanges is probably as shown by BRINK and COOPER (1931) in maize. Six kinds of spores can be produced at reduction division of the germ cells in heterozygous translocation individuals. In plants four types of spores, not having a complete chromosomal complement (heteroploid) are non-viable. The other two kinds of spores (orthoploid) are normal and reciprocally translocated respectively, and the eggs and sperm they produce are capable of forming viable zygotes. Thus the translocation is transmitted to 50 percent of the sporophytic offspring. In animals heteroploid eggs and sperm are viable but the zygotes derived from union of heteroploid and normal gametes are generally lethal.

Translocation heterozygotes would be 67 percent sterile if the six possible types of gametes were produced with equal frequency. However, the four types of gametes which produce non-viable young when combined with normal gametes are the result of the non-disjunction of chromosomes or chromosomal parts at meiosis, and their frequency, therefore, depends on the frequency of non-disjunction (DOBZHANSKY 1941). KOLLER (1944) summarized the breeding and cytological evidence of translocations in several species. He points out that the ratio of orthoploid to heteroploid gametes may vary considerably, not only between species, but also within species.

In the strain of rats reported in this study the fertility of all partially sterile rats was about 43 percent of normal, which would indicate that the proportion of orthoploid to heteroploid gametes does not deviate greatly from a 1:1 ratio. On the assumption of a 1:1 ratio and equal frequency of heteroploid gametes the mating of translocation heterozygotes *inter se* would result in 31 percent viable embryos. The actual observed results of six matings of partially sterile males to partially sterile females showed that the normal embryos accounted for 16 percent of the total ova. When this figure (16 percent) is compared with the fertility of normal testers, these partially sterile matings *inter se* were 20 percent as fertile as the normal tester matings.

SUMMARY

The inheritance of partial sterility in one strain of rats has been investigated by breeding tests on 156 male and female rats. This partial sterility is characterized by the uterine resorption of approximately 60 percent of the progeny of partially sterile sires or dams. The fertility (percentage of total ova that become normal embryos) of the partially sterile rats is about 43 percent of that of the normal tester rats. The trait is transmitted to about 50 percent of the living progeny of the rats that exhibit the trait. The most tenable hypothesis is that the partially sterile rats are heterozygous for a translocation.

LITERATURE CITED

- ALLEN, E., and E. C. MACDOWELL, 1940 Variation in mouse embryos of 8 days gestation. *Anat. Rec.* **77**: 165-174.
- BRINK, R. A., and D. C. COOPER, 1931 The association of semisterile-1 in maize with two linkage groups. *Genetics* **16**: 595-628.
- BOURICUS, J. K., 1948 Embryological and cytological studies in rats heterozygous for a probable reciprocal translocation. *Genetics* **33**: 577-587.
- BURACK, E., J. M. WOLFE, and A. W. WRIGHT, 1939 Prolonged vaginal bleeding and fetal resorption in the Albany strain of rats. *Anat. Rec.* **75**: 1-18.
- DOBZHANSKY, T., 1941 *Genetics and the origin of species*. 2nd edition. IX+446 pp. New York, New York: Columbia University Press.
- EVANS, H. M., and K. S. BISHOP, 1923 On the relations between fertility and nutrition. III. The normal reproductive performance of the rat. *J. Metab. Res.* **3**: 201-231.
- GREGORY, P. W., 1932 The potential and actual fecundity of some breeds of rabbits. *J. Exp. Zool.* **62**: 271-285.
- HAMILTON, W. J., JR., 1941 Reproduction of the field mouse. *Cornell A. E. S. Memoir* 237.
- HAMMOND, J., 1921 Further observations on the factors controlling fertility and fetal atrophy. *J. Agr. Sci.* **11**: 337-366.
- 1934 The inheritance of fertility in the rabbit. *Harper Adams Util. Poult. J.* **19**: 557.
- 1941 Fertility in mammals and birds. *Biol. Reviews* **16**: 165-190.
- HENSEN, M., 1942 The effect of roentgen irradiation of sperm upon the embryonic development of the albino rat. *J. Exp. Zool.* **91**: 405-433.
- HERTWIG, P., 1935 Über Sterilitätserscheinung bei röntgenbestrahlten Mäusen und deren Nachkommenschaft. *Z. I. A. V.* **70**: 517-523.
- 1938 Unterschiede in der Entwicklungsfähigkeit von F₁-Mäusen nach Röntgenbestrahlung von Spermatogonien, fertigen und unfertigen Spermatozoen. *Biol. Zbl.* **58**: 273-301.
- 1940 Vererbare Semisterilität bei Mäusen nach Röntgenbestrahlung verursacht durch reziproke Chromosomentranslokationen. *Z. I. A. V.* **79**: 1-29.
- HINMAN, R. B., 1933 Foetal resorption in animal husbandry. *Proc. Amer. Soc. Anim. Prod.* for 1932: 282-283.
- IBSEN, H. L., 1928 Prenatal growth in guinea-pigs, with special reference to environmental factors affecting weight at birth. *J. Exp. Zool.* **51**: 51-91.
- JONES, E. E., 1922 The genetic significance of intra-uterine sex ratios and degenerating fetuses in the cat. *J. Hered.* **13**: 237-239.
- KIRKHAM, W. B., 1917 Embryology of the yellow mouse. *Proc. Amer. Soc. Zool. Anat. Rec.* **11**: 480-481.
- 1919 The fate of homozygous yellow mice. *J. Exp. Zool.* **28**: 125-136.
- KOLLER, P. C., 1944 Segmental interchange in mice. *Genetics* **29**: 247-263.
- KOLLER, P. C., and C. A. AUERBACH, 1941 Chromosome breakage and sterility in the mouse. *Nature* **148**: 501-502.

- LONG, C. N. H., and A. S. PARKES. 1924 On the nature of foetal re-absorption. *Biochemical Jour.* **18**: 800-805.
- MACDOWELL, E. C., 1924 A method of determining the prenatal mortality in a given pregnancy of a mouse without affecting its subsequent reproduction. *Anat. Rec.* **27**: 329-336.
- SNELL, G. D., 1933 X-ray sterility in the male house mouse. *J. Exp. Zool.* **65**: 421-441.
- 1935 The induction by X-rays of hereditary changes in mice. *Genetics* **20**: 545-567.
- 1946 An analysis of translocation in the mouse. *Genetics* **31**: 157-180.
- WALETZKY, E., and R. D. OWEN, 1942 A case of partial sterility and embryonic mortality in the rat. *Rec. Genetics Soc. Amer. Genetics* **27**: 173.

EMBRYOLOGICAL AND CYTOLOGICAL STUDIES IN RATS
HETEROZYGOUS FOR A PROBABLE RECIPROCAL
TRANSLOCATION

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There have been no reports of spontaneously occurring reciprocal translocations in mammals. However, it is known that such aberrations may be produced with X-rays or other mutagens. SNELL (1935, 1939) and SNELL, BODEMANN, and HOLLANDER (1934) found it possible to increase greatly the percentage of embryonic deaths by treating male mice with X-rays or neutrons shortly before mating. It was found that approximately one half of the surviving offspring of these mice also produced small litters when mated to normal mice. A study of the descendants of one X-rayed mouse revealed approximately 42 percent non-viable embryos. Semisterility in mice was also produced by HERTWIG (1940) with X-rays. She found that the reduced litter sizes resulted from death of the embryos both before and after implantation. The majority of the abnormal embryos died shortly after implantation. The deaths were attributed to unbalanced gametes resulting from a reciprocal translocation.

KOLLER and AUERBACH (1941) used SNELL'S X-ray technique on mice and produced three individuals having semisterile offspring. They were able to identify an association of four chromosomes at meiosis in each of the three lines. In two of the lines the chromosomes formed a chain, and in the third they formed a ring. Such configurations were considered to provide adequate proof that a translocation had occurred.

Male rats were X-rayed by MARGARET HENSON (1942) who found that approximately 50 percent of the embryos resulting from matings of these rats to normal females underwent resorption during or immediately after implantation. She does not state whether any of the living offspring also produced small litters.

HISTORY OF PARTIALLY STERILE RATS

WALETZKY, in 1941, found a single hooded male rat that sired abnormally small litters when mated to normal females. Approximately 50 percent of the offspring of this male also produced small litters. Studies of the descendants of this male were made by WALETZKY and OWEN (1941) and by TYLER and CHAPMAN (1948). In the work of TYLER and CHAPMAN individuals were diagnosed as partially sterile or normal on the basis of a study of resorption rates of embryos. Normal females were mated to partially sterile males and laparotomized between the 11th and 16th days of pregnancy. Fifty-eight percent of the embryos in these females were undergoing resorption. The embryos undergoing

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resorption could be recognized by the small size of their implantation sites. These sites did not increase significantly in size after the 11th day. The average litter size of normal rats was approximately 8.0, whereas the average number of normal embryos per litter from semisterile rats was 3.0. In 118 control matings only 8.5 percent of the embryos examined were in process of resorption. If 8.5 percent of the embryos in all matings undergo resorption due to unknown causes, then approximately 50 percent of the embryos in matings of partially sterile \times normal are undergoing resorption due to what is believed to be a reciprocal translocation.

This paper is a report of embryological and cytological studies of the strain of partially sterile rats studied by TYLER and CHAPMAN. A total of nine partially sterile males was used. Twenty two matings of these males to normal females resulted in about 57.5 percent resorption, whereas there were only 6.5 percent resorptions in the control group (table 1). Slightly over half of the embryos that implanted underwent resorption. This is consistent with the results of 50 percent additional resorption as reported by TYLER and CHAPMAN.

It will be noticed in table 1 that the total number of implantation sites is slightly greater in the controls than in females mated to partially sterile males. This difference is not significant, but is in agreement with the observation of TYLER and CHAPMAN that between nine and ten percent of the eggs ovulated failed to implant.

TABLE 1
Data on litters.

	NUMBER OF LITTERS	AVERAGE NUMBER OF NORMAL EMBRYOS PER LITTER	AVERAGE NUMBER OF RESORPTIONS PER LITTER	TOTAL NUMBER OF IMPLANTA- TION SITES PER LITTER	% RESORPTION
Control matings of normal rats	16	8.9	0.6	9.5	6.5
Matings of partially sterile males \times normal females	22	3.7	5.0	8.7	57.5

The average litter size of nine partially sterile females was also very close to that of the partially sterile males tested. One of these females was mated four times to partially sterile males. Of these matings one produced three offspring, two produced one offspring each, and the fourth produced no young at all. None of these young was tested for sterility. It is therefore impossible to say whether a homozygous individual might be produced.

Thirty-five offspring from partially sterile \times normal matings were tested for sterility by matings to normal rats. Of these, 16 were classed as partially sterile and 19 as normal.

METHODS

Rats were diagnosed as normal or partially sterile by matings to two or more rats of normal parentage. With the aid of palpations and frequent observations during parturition the number of young born was determined with a fairly high degree of accuracy. Within five days after parturition simple laparotomy revealed the total number of decidual sites. The number of sites in excess of the number of young born was considered to be the number of embryos that had undergone resorption.

Partially sterile females were laparotomized in only a few cases. Evidence of the partial sterility was obtained only from average litter sizes.

Studies of the abnormal embryos were made by mating normal females to males known to be partially sterile. The females were placed with the males overnight when vaginal smears indicated they were in heat. If sperm were found in the smears the following morning, the females were later killed or laparotomized. Stages from the third to the fifth days were studied by pressing the embryos from the oviduct or flushing them from the uterus in physiological saline or Krebs' solution. The composition of Krebs' solution is as follows (given in g per 100 cc.): NaCl, 0.772; KCl, 0.023; CaCl₂, 0.0122; MgSO₄, 0.0191; Glucose, 0.20. This solution is buffered to pH 7.4. Fresh, unstained ova were photographed in the saline. Sections of the oviduct fixed in Zenker's formol gave reasonably good preparations of these early stages. For later stages the entire uterus was fixed in Zenker's or a mixture of picric acid, formic acid, and formalin (LILLIE 1944). Most of the sections were stained with Harris' haematoxylin and eosin. Zenker's gave the better preparations of all stages under six days.

Cytological studies were made of seminiferous tubules fixed in Carnoy's and stored in 70 percent alcohol. Temporary slides were prepared by the acetocarmine smear technique. It was found that the cells could be spread easily if the tubules were fixed in Carnoy's that had been warmed to 60°C. Long periods of storage in alcohol hardened the tubules to the extent that it was very difficult to obtain good spreading of the cells. The staining darkened and considerably improved during the first few weeks after the slides were prepared.

DESCRIPTION OF ABNORMAL EMBRYOS

A total of 208 embryos from matings of normal females × partially sterile males, and 83 control embryos, was examined microscopically. The ages of the embryos were measured from the time sperm were found in the vaginal smear of the mother. The day that sperm were found was considered the first day of pregnancy.

Fertilized eggs, two-cell stages, and a few unfertilized eggs were found on the third day of pregnancy both in females mated to partially sterile males and in control females. The only abnormality found at this stage was a two-cell embryo found in the controls. One of its two cells was disintegrating, whereas the other was apparently normal.

Most of the ova are capable of undergoing at least one cell division, and

usually two, without showing any abnormalities. It is possible that mitotic abnormalities are present in some cases even in the first division, but these could not be detected. The earliest signs of abnormality appear on the fourth day. Abnormalities at this stage usually appear as a marked inequality in the sizes of the blastomeres (figure 1). Some embryos show disintegrating cells, and some have oddly shaped extracellular particles lying within the zona pellucida. Figure 2 shows a normal embryo at this stage.

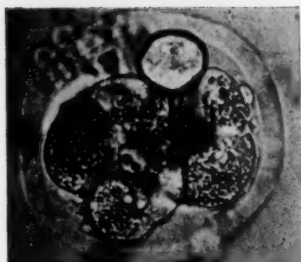
Normal embryos on the 5th day show the formation of a cavity, the blastocoel, near one end of the morula. The cavity elongates and the cell mass at the opposite end is called the ectoplacental cone. This cone also elongates, pushing into the blastocoel to form the ectodermal node. The layer of cells around the rest of the blastocoel becomes very thin and is called the trophoblast.

Abnormal embryos on the fifth day still show an inequality of the blastomeres (fig. 3). In some cases no blastocoel is formed. In others it forms but is very small. Some embryos appear to have two cavities forming; in others there are large vacuoles in the cells. Two embryos showed large extracellular particles lying inside the zona. The nature of these particles was not determined. Figure 4 shows an example of a normal litter mate of some of the abnormal embryos of this stage.

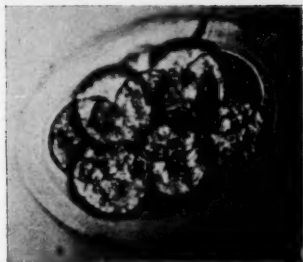
All of the embryos on the fifth day were found free in the lumen of the uterus, whereas all of those examined previous to this time were found in the oviduct. Very few embryos could be flushed from the uterus on or after the sixth day. Sectioning the uteri disclosed the embryos lying in deep grooves in the uterine wall, but not in contact with the maternal tissue. Figures 5 and 6 show abnormal and normal embryos, respectively, from the same litter on this day. If the cavity seen in figure 6 is the blastocoel, this embryo is oriented incorrectly, as the ectoplacental cone is then pointing toward the antimesometrial side of the uterus instead of away from it as in normal rat embryos. Another abnormal embryo of this age shows a cavity similar to the one seen here, but also has another cavity in the normal position. Most of these embryos show a cavity of some sort, but have little organization of the cells.

The normal embryo on the seventh day has begun to implant in the antimesometrial side of the uterine wall (fig. 7). The uterine epithelium has thinned and is beginning to disappear in this region. The trophoblast cells appear to be working their way into the decidual area. The ectodermal node is growing into the blastodermic cavity and is almost completely surrounded by a layer of visceral endoderm. In some cases a few cells of parietal endoderm may be seen lying just inside the trophoblast cells. These are the cells thought to give rise to the outer wall of the yolk sac. The abnormal embryo is also implanting at this time but no trophoblast can be distinguished (fig. 8). The embryo is not dead, as evidenced by the mitotic figure, but shows little organization. By this time abnormal embryos could readily be identified.

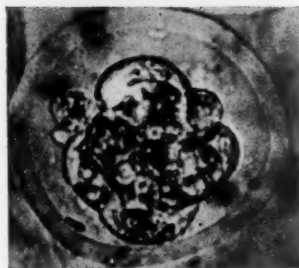
It is apparent that the majority of the abnormal embryos are capable of stimulating the normal response in the uterus. However, according to the data of TYLER and CHAPMAN, a small percentage may die before implantation or some of the abnormal gametes may be incapable of fertilization. The former



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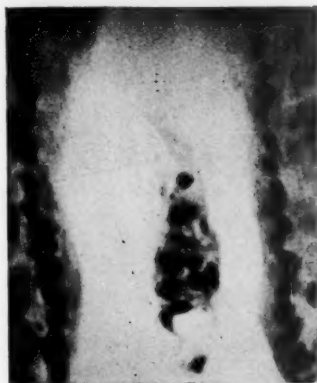
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6

FIGURE 1. Abnormal embryo from normal female mated to partially sterile male. Fourth day of pregnancy. Note inequality in sizes of blastomeres. $\times 390$.

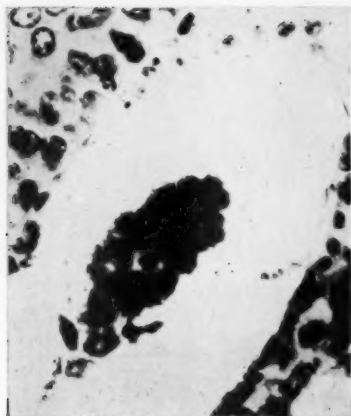
FIGURE 2. Embryo from normal female mated to normal male. Fourth day of pregnancy. $\times 390$.

FIGURE 3. Abnormal embryo from normal female mated to partially sterile male. Fifth day of pregnancy. No blastocoel is apparent. $\times 390$.

FIGURE 4. Normal embryo from normal female mated to partially sterile male. Fifth day of pregnancy. Note well formed blastocoel. $\times 390$.

FIGURE 5. Cross section of uterus of normal female mated to partially sterile male. Sixth day of pregnancy. Note abnormally placed cavity in embryo. $\times 390$.

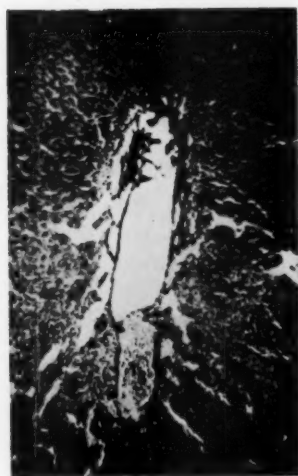
FIGURE 6. Cross section of uterus of normal female mated to partially sterile male. The embryo appears to be normal. Sixth day of pregnancy. $\times 390$.



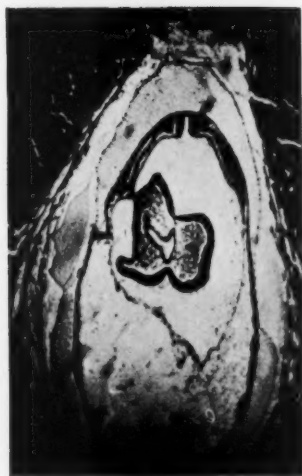
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FIGURE 7. Cross section through normal embryo implanting in uterus of normal female mated to partially sterile male. Seventh day of pregnancy. $\times 390$.

FIGURE 8. Cross section through abnormal embryo implanting in uterus of normal female mated to partially sterile male. Seventh day of pregnancy. Note mitotic figure indicated by arrow, and complete lack of cell differentiation. $\times 390$.

FIGURE 9. Cross section through uterus of normal female mated to partially sterile male. The embryo has been completely resorbed. Tenth day of pregnancy. Same magnification as figure 10. Note the few large cells possibly of embryonic origin. $\times 95$.

FIGURE 10. Cross section through uterus showing normal embryo on tenth day of pregnancy. Same magnification as figure 9. $\times 95$.

seems quite probable in view of the fact that some of the ova manifest abnormalities as early as the four or eight cell stages and may die before the time of implantation.

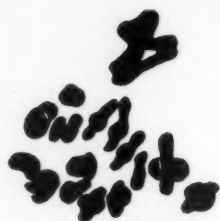
The ectodermal node is very much elongated by the eighth day. The trophoderm is scarcely visible, but the parietal endoderm forms an almost complete lining. The proamniotic cavity is forming in the egg cylinder and in some cases an inward fold of the wall of this cavity indicates the formation of the primitive groove. In abnormal embryos all that remains of the embryonic tissue are a few very large cells. However, the decidual cells of the uterus are continuing to develop in an apparently normal manner. One abnormal embryo was found in the controls at this stage. It presented much the same picture as those of the partially sterile rats.

As indicated by TYLER and CHAPMAN, embryos undergoing resorption could be differentiated from normal ones on the basis of size of the implantation sites any time after the 11th day of pregnancy. Figures 9 and 10 show sections of abnormal and normal sites, respectively. The abnormal sites were described by WALETZKY and OWEN (1941) as solid moles. Sectioning of six of these sites between the 10th and 19th days of pregnancy revealed normal decidual tissue present in the uterus. Leucocytes were present in the lumen and among the surrounding cells. These increased in number throughout pregnancy. No embryonic tissue was present in any of these sites except for certain large cells called giant cells or wandering cells. Figure 9 shows four of these cells. HUBER (1915) considers these cells to be merely specialized decidual cells, though they are now more commonly considered to be persisting cells of the deteriorating trophoderm which, in normal embryos, penetrates the uterine mucosa in the process of implantation. As pointed out earlier, the abnormal embryos studied never show any well-differentiated trophoderm. However, certain large cells, very probably of embryonic origin, are present in resorbing sites as late as the eighth day. If these cells are not phagocytized, but continue to reproduce themselves, they may account for the presence of rather large numbers of giant cells at the 19th day. If, on the other hand, these cells die with the rest of the embryonic tissue, the large cells seen in the later stages must be of maternal origin.

It will be seen from table 2 that the percentage of abnormal embryos increases with the duration of pregnancy. This may indicate that there are different types of abnormalities, manifesting themselves at different stages of development, but it is more probably due to the difficulties involved in recognizing abnormalities in the early stages.

WALETZKY and OWEN (1941) speak of grossly abnormal fetuses found late in pregnancy, but in this work no evidence of such fetuses has been found. No abnormal fetuses were found in any of six females laparotomized between the 12th and 19th days of pregnancy. No aborted fetuses or abnormal young were found, and in females laparotomized within five days after parturition there were no very large placental sites such as might have been expected if rather large fetuses had been undergoing resorption.

The resorbing embryos obtained from these rats differ considerably from the



11



12

FIGURE 11. Camera lucida drawing of metaphase chromosomes in primary spermatocyte of partially sterile rat.

FIGURE 12. Camera lucida drawing of metaphase chromosomes in primary spermatocyte of normal rat.

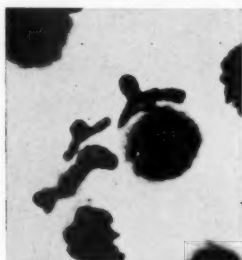


FIGURE 13. Photographs of the large configuration seen in primary spermatocytes of partially sterile rats. $\times 1200$.



FIGURE 14. Photographs of the largest bivalent in the primary spermatocytes of normal rats. $\times 1200$.

TABLE 2

Percentages of abnormal embryos found from the third to the eighth days of pregnancy.

DAY OF PREGNANCY ON WHICH EMBRYOS WERE EXAMINED	EMBRYOS FROM MATINGS OF NORMAL FEMALES TO SEMISTERILE MALES				CONTROLS		
	TOTAL NO. EXAMINED	NO. AP-PARENTLY NORMAL	NO. GROSSLY ABNORMAL	% AB-NORMAL	TOTAL NO. EXAMINED	NO. AP-PARENTLY NORMAL	NO. AB-NORMAL
3	22	22	0	0	21	20	1
4	55	43	12	28	8	8	0
5	71	53	18	34	31	31	0
6	24	15	9	33	13	13	0
7	13	8	5	38	5	5	0
8	10	5	5	50	5	4	1

abnormal mouse embryos that SNELL showed to result from X-ray produced translocations. They do, however, greatly resemble the resorptions described by HENSON (1942). It seems probable that some of the abnormal embryos shown by HENSON also resulted from X-ray produced translocations.

The foregoing description of the abnormal embryos tells us very little about the actual cause of death. The general pattern of death and resorption is rather strikingly similar to that of homozygous yellow mice described by KIRKHAM (1919) and also to the condition produced by BLANDAU and JORDAN (1941) in rats by delayed fertilization of the ovum. ROBERTSON (1942) states that, contrary to the opinion of KIRKHAM, homozygous yellow mice do not show abnormalities until after formation of the blastocyst, which makes the picture differ somewhat from that described here. As it is difficult to relate these three causes it may be that this is merely a typical pattern of death and resorption appearing in any case in which abnormalities occur at a very early stage.

CYTOLOGICAL EVIDENCE

As the breeding data of these partially sterile rats suggest the presence of a reciprocal translocation, it was thought desirable to examine the spermatozoa for evidence of an association of four chromosomes. On the basis of previous work (BELLING 1914; BRINK and COOPER 1931; KOLLER and AUERBACH 1941 and others) such an association might be expected to take the form of a chain or a ring.

Meiotic chromosomes of three semisterile males and of three normal males were examined. A heteromorphic pair resembling the X and Y chromosomes as shown by other workers (PINCUS 1927; BRYDEN 1932; ALLEN 1940; and KOLLER and DARLINGTON 1934) was identified in each of these rats (see figures 11 and 12). These chromosomes were usually seen joined end to end at

metaphase. Other configurations similar to those shown by PINCUS and by BRYDEN were also seen, and it was possible to identify 21 bivalents in the better plates of more than seven cells in the normal rat (fig. 12). This number is in agreement with that reported by MINOUCHI (1922), PINCUS (1927), and BRYDEN (1932).

In a total of 14 cells from the three partially sterile rats 19 bivalents were counted, plus a large configuration not seen in the normal rat. Examples of this configuration are shown in figures 11 and 13. The largest chromosome of the normal rat is shown in figure 14 for comparison.

No explanation other than that of a reciprocal translocation has been advanced to explain the breeding data obtained with these rats. As the large configuration shown here appears to be the only visible difference between the

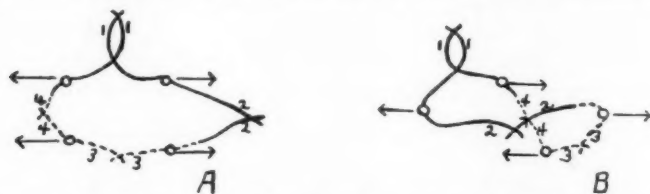


FIGURE 15. Diagram showing a possible interpretation of the large metaphase configuration seen in the primary spermatocytes of the partially sterile rats.

chromosomes of the normal and partially sterile rats, it seems probable that it is actually a quadrivalent involving two translocated and two normal chromosomes. The largest diplotene configuration appears to involve more than two chromosomes, for at least six chromosome ends can be seen. Although good diplotene preparations were difficult to obtain it was possible in some cases to see that the large configuration consisted of at least three, and probably four, chromosomes. In many cases the chiasmata were probably so well terminalized that the chromosome ends were not visible. A possible interpretation of the configuration is shown in figure 15. If a large chromosome, 1-2, exchanged a segment with a smaller chromosome, 3-4, the resulting chromosomes could appear at metaphase as shown in 15A or 15B. A twist such as shown in 15B would result in segregation so as to produce two other types of gametes, making a total of four possible gametes. Such a twist was frequently seen. It is recognized that this explanation may be somewhat different from the actual case, for it has been impossible to determine the positions of the centromeres with any certainty.

SUMMARY

Embryological and cytological studies have been made of rats the breeding data of which indicate them to be heterozygous for a reciprocal translocation of spontaneous origin.

Of the total number of embryos that become implanted in normal females mated to heterozygous males over 50 percent die on about the eighth day of pregnancy. Abnormalities appear as early as the third day when the ova have reached the four and eight cell stages. It seems likely that a few of these ab-

normal embryos do not survive until implantation.

The earliest signs of abnormality are extracellular particles and an inequality in the sizes of the blastomeres. No cell differentiation occurs, but the embryos are nevertheless capable of inducing the normal response in the uterine mucosa.

The primary spermatocytes of the heterozygous males show a large configuration not found in the normal rats, and therefore probably associated with the partial sterility. A possible interpretation of this configuration has been given. It is believed to be the expected quadrivalent involving two normal and two translocated chromosomes.

ACKNOWLEDGEMENTS

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LITERATURE CITED

- ALLEN, E., 1940 Variations in accessory chromosomes in metaphase and anaphase of the first spermatocytes of the albino rat. *J. Morph.* **66**: 453-462.
- BELLING, J., 1914 Inheritance of semi-sterility. *Z.I.A.V.* **12**: 303-342.
- BLANDAU, R. J., and E. S. JORDAN, 1941 The effect of delayed fertilization on the development of the rat ovum. *Amer. J. Anat.* **68**: 275-291.
- BRINK, R. A., and D. C. COOPER, 1931 The association of semisterile-1 in maize with two linkage groups. *Genetics* **16**: 595-628.
- BRYDEN, W., 1932 Cytogenetic studies on the rat. *J. Genetics* **26**: 395-415.
- HENSON, MARGARET, 1942 The effect of Roentgen irradiation of sperm upon the embryonic development of the albino rat. *J. Exp. Zool.* **91**: 405-433.
- HERTWIG, P., 1940 Vererbare Semisterilität bei Mäusen nach Röntgenbestrahlung, verursacht durch reziproke Chromosomentranslokationen. *Z.I.A.V.* **79**: 1-27.
- HUBER, G. C., 1915 Development of the albino rat. I. From pronuclear stage to the stage of mesoderm anlage; end of the first to end of the ninth day. *J. Morph.* **26**: 247-358.
- KIRKHAM, W. B., 1919 The fate of homozygous yellow mice. *J. Exp. Zool.* **28**: 125-135.
- KOLLER, P. C., and C. A. AUERBACH, 1941 Chromosome breakage and sterility in the mouse. *Nature* **148**: 501-502.
- KOLLER, P. C., and C. D. DARLINGTON, 1934 The genetical and mechanical properties of the sex chromosomes. I. *Rattus norvegicus*, ♂. *J. Genetics* **29**: 159-173.
- LILLIE, D. R., 1944 Picroformaldehyde formic acid for fixation. *J. Tech. Methods* **24**: 35-52.
- MINOUCHI, OSAMU, 1922 Spermatogenesis of the albino rat. *Jap. J. Genetics* **1**: 235-254.
- PINCUS, G., 1927 A comparative study of the chromosomes of the Norway rat and the black rat. *J. Morph.* **44**: 515-538.
- ROBERTSON, G. GORDON, 1942 An analysis of the development of homozygous yellow mouse embryos. *J. Exp. Zool.* **89**: 197-231.
- SNELL, G., 1935 Induction by X-rays of hereditary changes in mice. *Genetics* **20**: 545-567.
- 1939 Induction by irradiation with neutrons of hereditary changes in mice. *Proc. Nat. Acad. Sci.*, **25**: 11-14.
- SNELL, G., E. BODEMANN, and W. HOLLANDER, 1934 A translocation in the house mouse and its effect on development. *J. Exp. Zool.* **67**: 93-104.
- TYLER, W. J., and A. B. CHAPMAN, 1948 Genetically reduced prolificacy in rats. *Genetics* **33**: 565-576.
- WALETZKY, E., and R. D. OWEN, 1942 A case of inherited partial sterility and embryonic mortality in the rat. *Rec. Genetics Soc. Amer.* **10** (1941). *Genetics* **27**: 173.

GENETICS OF NATURAL POPULATIONS. XVIII. EXPERIMENTS
ON CHROMOSOMES OF *DROSOPHILA PSEUDOOBSCURA*
FROM DIFFERENT GEOGRAPHIC REGIONS

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THE PROBLEM

Sixteen different gene arrangements have been recorded in the third chromosomes of natural populations of *Drosophila pseudoobscura*, and eight in the third chromosomes of the related species *Drosophila persimilis*. Representatives of the same species which carry different types of third chromosomes have different adaptive values in some environments. If artificial populations with certain proportions of the chromosomal types are set up in population cages, these proportions may undergo rapid changes. Analysis of these changes leads to the inference that the adaptive values of individuals carrying two chromosomes of different types (structural heterozygotes) are higher than those of individuals with two similar chromosomes (structural homozygotes). The superior fitness of the heterozygotes results in populations reaching certain equilibrium states, at which the chromosomal types are present in definite proportions (WRIGHT and DOBZHANSKY 1946). Differential survival which favors structural heterozygotes relative to the homozygotes has been further ascertained through observations on deviations from the HARDY-WEINBERG equilibrium ratios of hetero- and homozygotes among flies which developed in population cages (DOBZHANSKY 1947a).

In the experiments previously reported, the experimental populations were made from flies the ancestors of which had been collected in a single locality—Piñon Flats, on Mount San Jacinto, in Southern California. The gene arrangements found in the third chromosomes of the Piñon Flats population occur, however, in populations of the Pacific Coast from British Columbia to Lower California. The problem naturally arises whether the adaptive properties of flies with the same chromosomes are alike wherever a given chromosomal type occurs, or whether the gene contents of these chromosomes are geographically differentiated. The flies used in the experiments to be reported in the present publication are descendants of wild flies collected in three different localities: Piñon Flats and Keen Camp, both on Mount San Jacinto in southern California, and Mather, in the Sierra Nevada of central California. It will be shown that chromosomes with the same gene arrangement found in geographically distinct populations have different adaptive properties.

MATERIAL

Progenitors of the flies that served as material for the experiments were collected at Piñon Flats and Keen Camp in April 1945 by MR. ALEXANDER SOKOLOFF, and at Mather during the summers of 1945 and 1946 by the writer.

Piñon Flats and Keen Camp are about 13 miles apart, at elevations of 4000 and 4300 feet respectively, but the biotic characteristics of the two localities are quite different (WRIGHT, DOBZHANSKY, and HOVANITZ 1942). Mather is some 300 miles north of the other localities, at elevation of 4600 feet, in the Transition Zone of the Sierra Nevada (DOBZHANSKY 1948).

The population cages used have been described by WRIGHT and DOBZHANSKY (1946); an improved model is shown in DOBZHANSKY 1947c.

PLAN OF THE EXPERIMENTS

A mixture of flies with desired proportions of two chromosomal types is introduced into a population cage and allowed to breed. At intervals of one or two months samples of eggs deposited in the cage are taken, and larvae hatched from them are raised under optimal conditions. When larvae mature, the chromosomes in their salivary glands are examined. Each "sample" consists of 300 chromosomes (150 larvae) divided into six "subsamples" of 25 larvae taken on six successive days. The frequencies of the chromosomal types present in the population of a cage at different times are thus determined. If changes in these frequencies are observed, they usually lead to the establishment of an equilibrium condition at which the two competing gene arrangements are present in the population in definite proportions. When the equilibrium is attained no further changes occur.

Since the process of selection results, in most experiments, in establishment of an equilibrium, the adaptive values of the structural heterozygotes must be higher than those of the corresponding homozygotes. For example, the fitness of Standard/Chiricahua heterozygotes is higher than that of Standard homozygotes and of Chiricahua homozygotes. If one of the homozygotes has an adaptive value equal to or higher than the heterozygotes, as is actually observed in one experiment (No. 31, table 7), the outcome of selection is eventually complete replacement of the less fit by the more fit chromosomal type. Mathematical analysis of the rates of change of the frequencies of gene arrangements in population cages permits estimation of the adaptive values of the chromosomal types involved (see equation 11 in WRIGHT and DOBZHANSKY 1946, also DOBZHANSKY 1947a). Taking the adaptive value (W) of the structural heterozygotes to be unity, those of the two homozygotes are $(1-s)$ and $(1-t)$ respectively, where s and t are selection coefficients. The frequency, q , at which equilibrium between the competing gene arrangements is established can be computed according to the simple formula, $\bar{q} = t/(s+t)$.

THE INITIAL POPULATIONS OF EXPERIMENTAL CAGES

Since flies carrying different gene arrangements in the third chromosome are phenotypically similar, the task of preparing mixtures of flies with desired proportions of gene arrangements to be placed in population cages is not a simple one. WRIGHT and DOBZHANSKY (1946) and DOBZHANSKY (1947a) set up series of pair matings of flies from strains of certain geographic origin, and examined cytologically several (8) larvae in the progeny of each pair. This permitted to infer the chromosomal constitution of the parents, and hence the

proportions of various chromosome types in the individual progenies. The adult flies that hatched were then placed in the population cages. This method has also been used in the experiments with chromosomes from Keen Camp described below (Cage Nos. 25-27, table 1).

TABLE 1
A review of the conditions in the different experiments.

CAGE NO.	ORIGIN	STARTED	TEMP.	LIGHT	NUMBER OF CHROMOSOMES				KINDS OF CHROMOSOMES			
					ST	AR	CH	TL	ST	AR	CH	TL
25	Keen	Nov. 6, 1945	25°	Dark	816	—	1650	—	10	—	13	—
26	Keen	Nov. 7, 1945	25°	Dark	619	1289	—	—	8	11	—	—
27	Keen	Nov. 9, 1945	25°	Dark	—	354	810	—	—	11	13	—
28	Mather	Dec. 22, 1945	25°	Dark	—	357	723	—	—	8	8	—
29	Mather	Dec. 22, 1945	25°	Dark	1119	485	—	—	8	6	—	—
30	Mather	Dec. 22, 1945	25°	Dark	566	—	1136	—	7	—	8	—
31	Mather	Dec. 23, 1945	25°	Dark	547	—	—	667	7	—	—	6
32	Mather	Dec. 24, 1945	25°	Dark	441	1837	—	—	8	10	—	—
33	Mather	Jan. 16, 1946	25°	Dark	—	1067	—	2061	—	6	—	7
34	Piñon	Feb. 25, 1946	Room	Light	2278	394	—	—	14	8	—	—
35	Piñon	Mar. 1, 1946	Room	Light	140	—	1172	—	10	—	11	—
36	Piñon	Mar. 2, 1946	Room	Light	240	1740	—	—	16	12	—	—
37	Piñon	Oct. 9, 1946	25°	Dark	—	370	1432	—	—	12	16	—
38	Piñon	Dec. 16, 1946	25°	Dark	—	2066	400	—	—	12	15	—
39	Mather	Oct. 9, 1946	25°	Dark	—	2345	543	—	—	10	16	—
40	Mather	Oct. 16, 1946	25°	Dark	—	374	2293	—	—	10	16	—
44	Piñon	Feb. 1, 1947	25°	Dark	—	1074	2594	—	—	13	15	—

In 1945 another method was adopted. Strains homozygous for various third chromosomes were prepared by means of a systematic inbreeding of flies from strains descended from wild progenitors. The progress of the inbreeding was controlled by cytological examination in each generation. Several dozen strains homozygous for the Standard, Arrowhead, Chiricahua, and Tree Line gene arrangements of Mather and of Piñon Flats origin were obtained. Population mixtures with any desired frequencies of the chromosomal types can be made by using different numbers of flies from various homozygous strains.

In every experiment six or more strains with the same gene arrangement were used to make up the initial population of a cage. The numbers of the strains used are shown in table 1 in the columns labelled "Kinds of Chromosomes." The numbers given are minimum estimates, since a strain homozygous for a given gene arrangement may contain two or even more different chromosomes with the same gene arrangement but with different complexes of polygenes. The structural homozygotes produced in the population cages are, thus, mostly genic heterozygotes which should have their fitness enhanced by hybrid vigor (for a discussion of this point see WRIGHT and DOBZHANSKY 1946, pp. 130-131). The numbers of flies which constituted initial populations of the experimental cages are given in table 1 in terms of numbers of chromosomes; a fly has, of course, two third chromosomes.

In most of the experiments, the population cages were kept at 25°C in a dark constant temperature room, or in incubators in which the only source of light were the incandescent bulbs used for heating. Some of the cages were, however, kept in laboratory or in apartment rooms with temperatures fluctuating between 21° and 27°C, and alternating light and darkness. The conditions in which the experiments were begun are summarized in table 1; the changes that were subsequently made in some of them are stated in the descriptions of the respective experiments.

The names of the Standard, Arrowhead, Chiricahua, and Tree Line gene arrangements are hereafter abbreviated to ST, AR, CH, and TL respectively.

CHROMOSOMES OF THE PIÑON FLATS POPULATION

WRIGHT and DOBZHANSKY (1946) and DOBZHANSKY (1947a) have reported eight experiments in which ST and CH chromosomes of Piñon Flats origin competed in population cages, and a ninth is reported in table 2 of the present article (No. 35). In two experiments (Nos. 9 and 17) the populations were kept in a cold room at 16½°C. No significant changes in the frequencies of ST or CH chromosomes took place in the cages kept at this temperature, just as no changes were observed in three other cages (Nos. 3, 7, and 16) which contained mixtures of ST, AR, and CH chromosomes and were kept at 16½°C. This shows that, in the environments prevailing in population cages kept at 16½°C, the adaptive values of homo- and heterozygotes for ST and CH chromosomes are not different enough to give rise to changes in the frequencies of these gene arrangements that would be easily noticeable within time intervals corresponding to several generations.

On the contrary, significant changes in the frequencies of ST and CH chromosomes were observed in each of the seven cages kept at 25° or at room temperature. Thus, cage No. 35 was started on March 1, 1946, with a population having about 11 percent ST and 89 percent CH chromosomes (table 2). Within a month, in early April, the frequency of ST chromosomes doubled, and by early May nearly trebled. In August ST chromosomes were more frequent than CH, and in late December the frequency of ST reached about 70 percent. The frequencies of 70–75 percent ST and 25–30 percent CH chromosomes seem to represent an equilibrium position for these chromosomes of Piñon Flats origin in population cages at 25°C. If a cage is started with an initial frequency of ST above, and of CH below, the equilibrium, CH increase and ST decrease in frequency (cage No. 24, DOBZHANSKY 1947a).

Since the competition of ST and CH chromosomes leads to establishment of equilibrium at which both competitors are present in the population, the adaptive value (*W*) of the ST/CH genotype must be higher than those of the ST/ST and CH/CH genotypes. From the experiments previously published by WRIGHT and DOBZHANSKY (1946) and DOBZHANSKY (1947a) the following estimates have been derived:

<i>Genotype</i>	<i>W</i>		
ST/ST	0.77	s=0.23	
ST/CH	1.00		$\hat{q}=0.73$
CH/CH	0.39	t=0.61	

From experiment No. 35 taken by itself rather different estimates of the selection coefficients are arrived at, namely:

<i>Genotype</i>	<i>W</i>		
ST/ST	0.85	$s=0.15$	
ST/CH	1.00		$\hat{q}=0.74$
CH/CH	0.58	$t=0.42$	

It is probable that the data obtained in cage No. 35 underestimate the magnitude of the selection coefficients, because this cage (and No. 36) was kept in a room in which the temperatures during most of April, May, and June averaged below 25°C. The length of a generation at these temperatures was longer than 3.5 weeks, which is the estimate used in the computations of the selection coefficients. Taking all the data into account (including cage No. 35), the estimates $s=0.19$, $t=0.53$, and $\hat{q}=0.74$ are obtained. It may be noted that all the estimates of \hat{q} agree in showing that the equilibrium frequency of ST chromosomes lies close to 74 percent, which is only slightly higher than actually obtained in experiments (72 percent in cage No. 19, 71 percent in cage No. 35).

TABLE 2
Percentage frequencies of the different gene arrangements in experiments involving chromosomes of Piñon Flats origin

TIME ¹	CAGE NO. 35		CAGE NO. 36		CAGE NO. 34	
	ST	CH	ST	AR	ST	AR
Feb. 25-Mar. 2, 1946	10.7	89.3	12.1	87.9	85.3	14.7
E. Apr., 1946	21.7	78.3	26.0	74.0	81.0	19.0
E. May, 1946	28.3	71.7	35.7	64.3	76.7	23.3
E. June, 1946	37.7	62.3	41.3	58.7	77.3	22.7
E. July, 1946	43.7	56.3	46.3	53.7	79.3	20.7
M. Aug., 1946	53.7	46.3	56.7	43.3	75.0	25.0
M. Sept., 1946	54.7	45.3	—	—	—	—
M. Oct., 1946	—	—	64.3	35.7	—	—
M. Nov., 1946	65.7	34.3	—	—	—	—
L. Nov., 1946	—	—	66.7	33.3	—	—
L. Dec., 1946	71.0	29.0	—	—	—	—
E. Jan., 1947	—	—	68.3	31.7	—	—
M. Feb., 1947	—	—	68.0	32.0	—	—

¹ E. = early; M. = middle; L. = late.

Three experiments have been made in which ST and AR chromosomes of Piñon Flats origin were present in population cages. One of these experiments has been reported by WRIGHT and DOBZHANSKY (1946, experiment No. 14), and two are shown in table 2, (cages Nos. 34 and 36). All three were carried at room temperature or at 25°C. In cages Nos. 14 and 36, the initial populations contained appreciably fewer ST than AR chromosomes. The frequency of ST rose rapidly in both cages. In cage No. 36 which was maintained for just under a year, the initial frequency of 12 percent was more than doubled in about 4.5

weeks, and reached about 65 percent in about 7 months; for the subsequent 4 months it advanced to only 68 percent, indicating an approach to equilibrium. Cage No. 34 had initially 85 percent of ST chromosomes; the observed changes were rather erratic but their trend was on the whole downward, reaching 75 percent after about six months. This also indicates an equilibrium frequency in the neighborhood of 70 percent. Estimates of the adaptive values arrived at on basis of all three experiments are as follows:

<i>Genotype</i>	<i>W</i>		
ST/ST	0.81	$s=0.19$	
ST/AR	1.00		$\hat{q}=0.72$
AR/AR	0.50	$t=0.50$	

AR and CH chromosomes of Piñon Flats origin were present in the populations of cages in five experiments (No. 15 in WRIGHT and DOBZHANSKY 1946, No. 23 in DOBZHANSKY 1947a, Nos. 37, 38, and 44 in table 3 of the present paper). Except for No. 15 which was kept at room temperature, the experiments were carried at 25°C.

TABLE 3

Percentage frequencies of AR and CH gene arrangements in experiments involving chromosomes of Piñon Flats origin.

TIME	CAGE NO. 37		CAGE NO. 38		CAGE NO. 44	
	AR	CH	AR	CH	AR	CH
Oct. 9-16, 1946	20.5	79.5	83.8	16.2	—	—
M. Nov., 1946	41.7	58.3	80.7	19.3	—	—
M. Dec., 1946	54.0	46.0	83.7	16.3	—	—
L. Jan., 1947	—	—	79.7	21.3	—	—
Feb. 1, 1947	—	—	—	—	29.3	70.7
L. Feb., 1947	—	—	75.0	25.0	—	—
E. Mar., 1947	—	—	—	—	40.7	59.3
L. Mar., 1947	—	—	75.3	24.7	—	—
M. May, 1947	—	—	—	—	55.3	44.7
L. June, 1947	—	—	—	—	58.3	41.7
L. July, 1947	—	—	—	—	74.0	26.0
L. Aug., 1947	—	—	—	—	76.7	23.3
M. Nov., 1947	—	—	—	—	75.0	25.0

In four experiments (Nos. 15, 23, 37, and 44) the initial populations had fewer AR than CH chromosomes. The frequencies of AR rose rapidly. In cage No. 44, which is the only one which was maintained sufficiently long for equilibrium frequencies to be approached, the frequency of AR rose to around 75 percent and remained there for about 4 months, after which the experiment was terminated (table 3). Cage No. 38 had initially about 84 percent of AR chromosomes; the frequency of AR declined slightly, and reached values between 75 and 80 percent, which are accordingly indicated as the location of the equilibrium of AR in competition with CH. Computations of the adaptive values from the data of the four experiments gave the following estimates:

<i>Genotype</i>	<i>W</i>		
AR/AR	0.86	$s=0.14$	
AR/CH	1.00		$\hat{q}=0.79$
CH/CH	0.48	$t=0.52$	

CHROMOSOMES OF THE KEEN CAMP POPULATION

A population cage (No. 25, table 4) was started, at 25°C in early November 1945, with 33 percent ST and 67 percent CH chromosomes of Keen Camp origin. By late February 1946, the frequency of ST rose to 70 percent, and by late March to 75 percent. No significant changes were observed for the next three months, indicating that an equilibrium has been approached or attained. On June 26, 1946 the cage was moved to a refrigerated room with a temperature of 16°C. Population samples taken in September and November failed to disclose significant alterations in the frequencies of the chromosomal types. It

TABLE 4
Percentage frequencies of the different gene arrangements in experiments involving chromosomes of Keen Camp origin.

TIME	TEMP.	CAGE NO. 25		CAGE NO. 26		CAGE NO. 27	
		ST	CH	ST	AR	AR	CH
Nov. 6-9, 1945	25°	33.1	66.9	32.4	67.6	30.4	69.6
M. Dec., 1945	25°	52.3	47.7	37.0	63.0	37.0	63.0
L. Jan., 1946	25°	56.3	43.7	52.3	47.7	41.3	58.7
L. Feb., 1946	25°	70.3	29.7	56.3	43.7	43.3	56.7
L. Mar., 1946	25°	75.0	25.0	60.3	39.7	—	—
L. Apr., 1946	25°	76.3	23.7	60.0	40.0	45.3	54.7
L. June, 1946	25°	76.3	23.7	60.3	39.7	—	—
E. Sept., 1946	16°	79.3	20.7	67.0	33.0	—	—
E. Nov., 1946	16°	79.0	21.0	60.0	40.0	—	—
E. Jan., 1947	16°	—	—	58.0	42.0	—	—

may be recalled that ST and CH homozygotes and heterozygotes of Piñon Flats origin possess equal adaptive values at 16°C; the behavior of the population No. 25 is compatible with the supposition that the Keen Camp chromosomes are, in this respect, like those from Piñon Flats. The adaptive values at 25°C, computed from the data in table 4, are as follows:

<i>Genotype</i>	<i>W</i>		
ST/ST	0.91	$s=0.09$	
ST/CH	1.00		$\hat{q}=0.86$
CH/CH	0.42	$t=0.58$	

The equilibrium point for ST chromosomes in competition with CH seems to be slightly higher for the chromosomes of Keen Camp origin than for the chromosomes of Piñon Flats origin (see page 591-592).

A mixture of about 32 percent of ST and 68 percent of AR chromosomes of Keen Camp origin was set in cage No. 26, at 25°C, in November 1945 (table

4). By March 1946 the frequency of ST reached 60 percent, and stayed there till June, indicating an equilibrium. On June 26, 1946 the cage was transferred to 16°C. In September, a sample showed 67 percent ST, but samples taken in November 1946 and January 1947 again contained about 60 percent ST. The adaptive values at 25°C are as follows:

<i>Genotype</i>	<i>W</i>		
ST/ST	0.79	$s=0.21$	$\hat{q}=0.67$
ST/AR	1.00		
AR/AR	0.58	$t=0.42$	

These estimates are probably not significantly different from those obtained for ST and AR chromosomes of Piñon Flats origin.

Cage No. 27 (table 4) was started in November 1945 with a population of 30 percent AR and 70 percent CH chromosomes from Keen Camp (at 25°C). AR chromosomes increased in frequency rather slowly, and reached 45 percent in April of 1946. The following estimates of the adaptive values are obtained:

<i>Genotype</i>	<i>W</i>		
AR/AR	0.54	$s=0.46$	$\hat{q}=0.47$
AR/CH	1.00		
CH/CH	0.60	$t=0.40$	

These values are very different from the estimates obtained for AR and CH chromosomes of Piñon Flats origin.

CHROMOSOMES OF THE MATHER POPULATION

The initial population in cage No. 30 contained about 33 percent of ST and 67 percent CH chromosomes derived from ancestors collected at Mather (table 5). During the eight and a half months which this cage was held at 25°C, the frequency of ST rose to about 77 percent and appeared to have approached an equilibrium. On September 12th, this cage was transferred to a cold room at 16°C. No significant change in the frequencies of the gene arrangements appeared until January of the following year. The adaptive values of the chromosomal types at 25°C are estimated as follows:

<i>Genotype</i>	<i>W</i>		
ST/ST	0.78	$s=0.22$	$\hat{q}=0.77$
ST/CH	1.00		
CH/CH	0.28	$t=0.72$	

These estimates are not very different from those obtained for ST and CH chromosomes of Piñon Flats origin if the experiment No. 35 is disregarded (cf. page 591-592).

Two experiments, Nos. 29 and 32 (table 5), involved ST and AR chromosomes of Mather origin. In No. 29, the initial population contained about 70 percent ST and 30 percent AR chromosomes. This cage was kept for about seven months at 25°C, and the frequency of ST chromosomes in its population declined to about 55 percent and seemed to reach an equilibrium at that value.

Cage No. 32 contained initially about 19 percent ST and 81 percent AR chromosomes (table 5). During the 8½ months when this cage was kept at 25°C the frequency of ST rose to between 50 and 55 percent, which appears to be close to the equilibrium frequency. The adaptive values of the chromosomal types in these cages at 25°C are as follows:

<i>Genotype</i>	<i>W</i>		
ST/ST	0.64	$s=0.36$	
ST/AR	1.00		$\hat{q}=0.54$
AR/AR	0.575	$t=0.425$	

It is evident that, with ST and AR chromosomes of Mather origin, the equilibrium frequency of ST is appreciably lower than it is with similar chromosomes of Piñon Flats and Keen Camp origin.

On September 17, 1946, after the population in cage No. 32 reached an equilibrium at a level of 50–55 percent of ST chromosomes, this cage was removed from the temperature 25° and transferred to a cold room at 16°C. Two

TABLE 5
Percentage frequencies of the different gene arrangements in experiments involving chromosomes of Mather origin.

TIME	TEMP.	CAGE NO. 29		CAGE NO. 32		CAGE NO. 30		CAGE NO. 28	
		ST	AR	ST	AR	ST	CH	AR	CH
Dec. 22, 1945	25°	69.8	30.2	19.4	80.6	33.3	66.7	33.1	66.9
L. Jan., 1946	25°	62.7	37.3	23.1	76.9	49.7	50.3	41.5	58.5
L. Feb., 1946	25°	56.3	43.7	30.0	70.0	62.7	37.3	44.7	55.3
L. Mar., 1946	25°	57.3	42.7	37.7	62.3	64.0	36.0	45.0	55.0
M. May, 1946	25°	58.7	41.3	44.7	55.3	71.3	28.7	39.7	60.3
L. June, 1946	25°	54.7	45.3	54.3	45.7	77.3	22.7	43.3	56.7
L. July, 1946	25°	54.0	46.0	49.7	50.3	72.7	27.3	—	—
E. Sept., 1946	25°	—	—	52.0	48.0	77.7	23.3	—	—
E. Nov., 1946	16°	—	—	44.7	55.3	74.7	25.3	—	—
M. Jan., 1947	16°	—	—	52.7	47.3	78.3	21.7	—	—
E. Mar., 1947	4°	—	—	56.0	44.0	—	—	—	—
M. June, 1947	4°	—	—	57.3	42.7	—	—	—	—

months later, in November 1946, the population sample taken proved to contain 45 percent ST, which represented an ostensible decrease. But in January 1947 the frequency of ST again rose to about 53 percent. These fluctuations seemed to indicate that the transfer from the high to the low temperature was followed by a drop in the frequency of ST, with a subsequent recovery. To test the possibility that exposure of the population to alternating high and low temperatures might modify the equilibrium frequencies of ST and AR chromosomes, between January 20 and mid-March 1947 the cage No. 32 was placed on alternate weeks in a dark cold room at 4°C and at room temperature in a room accessible to daylight. The sample taken in March 1947 disclosed no significant change (table 5). From mid-March to mid-June of 1947 the cage was placed overnight at 4°C and during the daylight hours at room tempera-

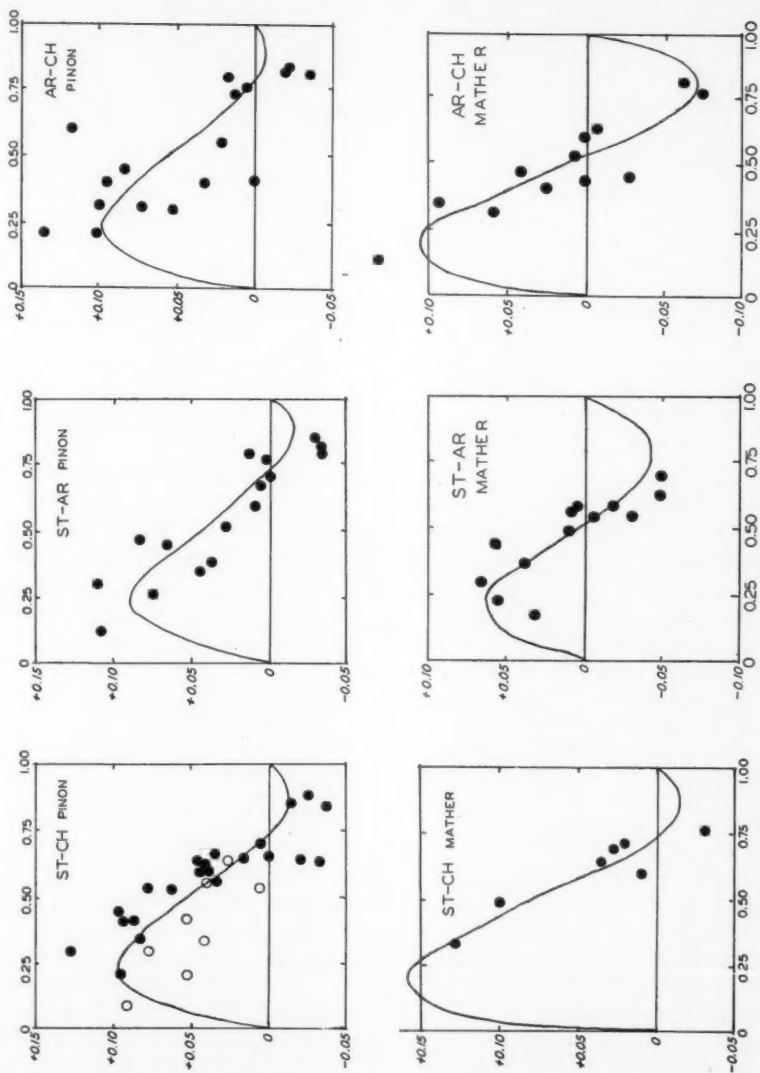


FIGURE 1. Increments of frequencies of ST (or AR) gene arrangements per generation in different experiments for different initial frequencies of the same gene arrangement (regression of Δq over q). Vertical axis—increments of frequencies (Δq); horizontal axis—initial frequencies (q). Dots—observed values; curves—theoretically computed values. The open circles in the diagram for ST-CH from Pinon Flats represent the data from the aberrant experiment in cage No. 35.

ture. No changes in the frequencies of ST and AR were observable in the sample taken in mid-June (table 5). The experimental population in this cage was about 18 months old when it was finally discarded.

TABLE 6
Percentage frequencies of AR and CH gene arrangements in experiments involving chromosomes of Mather origin.

TIME	CAGE NO. 39		CAGE NO. 40	
	AR	CH	AR	CH
Oct. 9-16, 1946	81.2	18.8	14.0	86.0
M. Nov., 1946	72.3	27.7	35.0	65.0
M. Dec., 1946	63.0	37.0	47.0	53.0
L. Jan., 1947	61.3	38.7	54.0	46.0
E. Apr., 1947	62.3	37.7	56.3	43.7

AR and CH chromosomes from Mather were involved in three experiments, all conducted at 25°C (No. 28, table 5, Nos. 39 and 40, table 6). In Nos. 28 and 40 the initial populations contained respectively 33 and 14 percent AR, and the frequencies of AR increased for several generations. In No. 39 a high frequency, 81 percent, of AR was initially present and it declined in the course of the experiment. Unfortunately none of the three experiments were carried long enough to be certain that equilibrium values were reached. The following estimates of adaptive values are obtained from the three experiments:

<i>Genotype</i>	<i>W</i>		
AR/AR	0.81	$s=0.523$	
AR/CH	1.00		$\hat{q}=0.534$
CH/CH	0.60	$t=0.599$	

Experiments Nos. 31 and 33 (table 7) involved chromosomes with the TL gene arrangement, in combinations with respectively ST and AR chromosomes, all of Mather origin. The unique feature of the experiment No. 31 is that no equilibrium was arrived at in the population concerned, and instead one of the gene arrangements has supplanted its competitor. The cage No. 31 had 45 percent of ST and 55 percent of TL chromosomes in the initial population in late December of 1945. By late March 1946, the frequency of ST rose to about 77 percent, by June to 89 percent, by September to 98 percent, and by November to 98.7 percent. It appears certain that TL chromosomes were headed for extinction. The experiment was discontinued because with very low frequencies of TL chromosomes the accidents of sampling in a limited population might vitiate the results. The adaptive values of the three genotypes involved in the experiment No. 31 are:

<i>Genotype</i>	<i>W</i>	
ST/ST	1.12	$s=-0.12$
ST/TL	1.00	
TL/TL	0.33	$t=0.67$

TABLE 7

Percentage frequencies of TL, ST, and AR gene arrangements in experiments involving chromosomes of Mather origin (at 25°).

TIME	CAGE NO. 31		CAGE NO. 33	
	ST	TL	AR	TL
Dec. 23, 1945	45.1	54.9	—	—
Jan. 16, 1946	—	—	34.1	65.9
L. Jan., 1946	62.3	37.7	—	—
M. Feb., 1946	—	—	57.7	42.3
L. Feb., 1946	71.7	28.3	—	—
M. Mar., 1946	—	—	64.7	35.3
L. Mar., 1946	77.3	22.7	—	—
M. Apr., 1946	—	—	68.7	31.3
M. May, 1946	82.0	18.0	69.3	30.7
L. June, 1946	89.0	11.0	66.0	34.0
L. July, 1946	93.0	7.0	75.3	24.7
E. Sept., 1946	98.0	2.0	74.3	25.7
E. Nov., 1946	98.7	1.3	80.0	20.0
M. Dec., 1946	—	—	76.0	24.0

Individuals homozygous for ST chromosomes have an adaptive value higher than the heterozygotes, while the TL homozygotes are semilethal.

Since individuals both homozygous and heterozygous for TL are inferior to ST homozygotes, the question naturally arises why are the TL chromosomes retained at all in natural populations instead of being eliminated by natural selection? Experiment No. 33 (table 7) supplies an answer, for it shows that TL chromosomes form highly adaptive heterozygotes with another normal constituent of the Mather population, namely AR. Cage No. 33 was started with a population of 34 percent AR and 66 percent TL chromosomes, and was kept at 25°C. The frequency of AR rose rapidly, and about six months later an equilibrium was seemingly attained at a level of about 75 percent AR. The estimates of the adaptive values are as follows:

<i>Genotype</i>	<i>W</i>		
AR/AR	0.69	$s=0.306$	
AR/TL	1.00		$\hat{q}=0.74$
TL/TL	0.12	$t=0.88$	

Compared to AR/TL heterozygotes, individuals homozygous for AR have an appreciably reduced fitness, while TL homozygotes are well in the semilethal range.

DISCUSSION

Because of the variation of the gene arrangement in the third chromosome of *Drosophila pseudoobscura*, natural populations of this species in some geographic regions are mixtures of structural heterozygotes and structural homozygotes. Structural heterozygotes carry two third chromosomes with different

gene arrangements, while homozygotes have chromosomes with similar gene orders. Experiments of WRIGHT and DOBZHANSKY (1946), DOBZHANSKY (1947a), and those reported in the present article, have shown that, at Piñon Flats and Keen Camp localities in southern California and at Mather in the Sierra Nevada, the structural heterozygotes are superior in fitness to the homozygotes. The adaptive superiority of the heterozygotes (heterosis) makes the populations very plastic, that is, able to respond by rapid adaptive changes to variations in environmental conditions. At the same time, natural selection prevents any of the gene arrangements from being eliminated from the populations altogether, which would reduce the adaptive plasticity of these populations.

The Tree Line (TL) gene arrangement from the Mather population is an exception to the rule of superior fitness of heterozygotes, because the heterozygotes for TL and Standard (ST) gene arrangements (TL/ST) are inferior to the ST/ST homozygotes, although superior to TL/TL homozygotes. Accordingly, in an experimental population consisting of TL and ST chromosomes the former have been wholly eliminated by natural selection. But this exception proves the rule, inasmuch as TL chromosomes form superior heterozygotes with Arrowhead (AR) chromosomes from the Mather locality, AR/AR and TL/TL homozygotes being inferior in adaptive value to AR/TL heterozygotes. TL chromosomes induce heterosis in combination with some but not with other chromosomes which exist in the same population. This explains both the retention of TL chromosomes in the Mather population, and the fact that they are relatively rare compared to ST, AR, and CH chromosomes.

Two hypotheses may be advanced regarding the genetic nature of the differences in fitness observed between the hetero- and homozygotes for various gene arrangements. First, each type of chromosome may carry a complex of polygenes different from those carried in other gene arrangements. The gene arrangements differ in inversions of chromosome sections; the inversions suppress most of the gene recombination in inversion heterozygotes (DOBZHANSKY and EPLING 1948), and thus bind together adaptively valuable polygene complexes which are inherited *en bloc*. Secondly, the rearrangement of genes in chromosomes may influence physiological traits of their carriers through position effects.

Several previously published facts favored, although they did not prove, the first of the above hypotheses. Chromosomes with the same gene arrangement found in geographically different populations behave differently (DOBZHANSKY 1943, 1947b, 1948). On Mount San Jacinto, in southern California, ST chromosomes are more frequent in the lower localities (Andreas Canyon and Piñon Flats) than in the higher one (Keen Camp), Chiricahua (CH) chromosomes show the opposite relationship with altitude and AR chromosomes do not change in frequency. In the Sierra Nevada of California the frequencies of ST decrease with altitude, AR increase, and CH change relatively little. At Andreas Canyon and Piñon Flats, the frequencies of ST chromosomes wane and those of CH wax from March to June, between June and September the reverse change occurs, while during fall and winter the relative frequencies of

all chromosomes remain stable. At Keen Camp, less than 15 miles away from Piñon and Andreas, no seasonal cyclic changes are observed, but the frequencies of ST continuously increased and those of AR and CH decreased for at least eight consecutive years. In the Sierra Nevada, ST chromosomes become more and AR less frequent as the summer progresses, with CH remaining relatively constant; the converse change which closes the cycle must occur in winter or early in spring.

In a large territory comprising parts of Arizona, New Mexico, Utah, and Colorado populations of *Drosophila pseudoobscura* consist preponderantly of homozygotes for AR chromosomes (DOBZHANSKY 1944). Yet, AR homozygotes (of California origin) had a far lower adaptive value than AR/ST, AR/CH, and AR/TL heterozygotes in our experiments. Despite the similarity in gene arrangements, AR chromosomes from California have different complexes of polygenes than AR chromosomes from Arizona and neighboring states.

The experiments described in the present article show in a conclusive manner that chromosomes with the same gene arrangement coming from localities even as close as Piñon Flats and Keen Camp (about 13 miles) may have different adaptive properties. Chromosomes from Mather, about 300 miles from Piñon and Keen, are again different. In another publication data will be presented that will show that in heterozygotes which carry chromosomes with different gene arrangements (such as ST and CH) from different localities (such as Piñon and Mather), heterosis disappears and the fitness of heterozygotes becomes equal to or lower than in the corresponding homozygotes. The adaptive properties of a chromosome are, consequently, determined not by the gene arrangement but by the quality of the genes it contains. This does not exclude the possibility that some position effects are, nevertheless, produced by the inversions, but the adaptive values of the chromosomes are not determined by position effects alone. The implications of this finding for the understanding of the evolution of the adaptive mechanisms in *Drosophila pseudoobscura* will be discussed elsewhere.

SUMMARY

Populations containing mixtures of Standard (ST), Arrowhead (AR), Chiricahua (CH) and Tree Line (TL) chromosomes have been maintained in population cages. In some experiments, the chromosomes were derived from progenitors collected at Piñon Flats, in others from Keen Camp, and in still others from Mather, California. The distance between Piñon Flats and Keen Camp is about 13 miles; between either of these two localities and Mather about 300 miles.

Regardless of the geographic origin, the structural (inversion) heterozygotes are superior in fitness to the corresponding structural homozygotes. Accordingly, the process of natural selection does not result in elimination of one and establishment of the other competing chromosome types; instead, an equilibrium is reached at which both competitors are retained with certain definite frequencies. This rule has two exceptions. First, when ST chromosomes from Mather compete with TL chromosomes from the same locality, the former

crowd out the latter entirely. Secondly, the differences in fitness between the chromosomal types are observed at 25°C, while at 16°C the adaptive values of these types are more nearly similar or even identical.

The adaptive values of the chromosomal types depend upon the geographic origin of the flies. Thus, AR/AR homozygotes are much superior in fitness to the CH/CH homozygotes of Piñon Flats origin, while AR/AR of Mather origin are only slightly superior to CH/CH from Mather. Similarly, ST/ST homozygotes are relatively much superior to AR/AR homozygotes if the chromosomes involved are of Piñon Flats origin than if they are of Mather origin. This shows that the chromosomes with the same gene arrangement found in different localities have different gene contents. In the population of any one locality, the gene contents of chromosomes with different gene arrangements are mutually adjusted by natural selection, so that highly adapted (heterotic) heterozygotes are produced.

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LITERATURE CITED

- DOBZHANSKY, TH., 1943 Genetics of Natural Populations. IX. Temporal changes in the composition of populations of *Drosophila pseudoobscura*. *Genetics* **28**: 162-186.
1944. Chromosomal races in *Drosophila pseudoobscura* and *Drosophila persimilis*. Carnegie Inst. Washington Publ. **554**: 47-144.
- 1947a Genetics of natural populations. XIV. A response of certain gene arrangements in the third chromosome of *Drosophila pseudoobscura* to natural selection. *Genetics* **32**: 142-160.
- 1947b A directional change in the genetic constitution of a natural population of *Drosophila pseudoobscura*. *Heredity* **1**: 53-64.
- 1947c Adaptive changes induced by natural selection in wild populations of *Drosophila*. *Evolution* **1**: 1-16.
- 1948 Genetics of natural populations. XIV. Altitudinal and seasonal changes produced by natural selection in certain populations of *Drosophila pseudoobscura* and *Drosophila persimilis*. *Genetics* **33**: 158-176.
- DOBZHANSKY, TH., and C. EPLING, 1948 The suppression of crossing over in inversion heterozygotes of *Drosophila pseudoobscura*. *Proc. Nat. Acad. Sci.* **34**: 137-141.
- WRIGHT, S., and TH. DOBZHANSKY, 1946 Genetics of natural populations. XII. Experimental reproduction of some of the changes caused by natural selection in certain populations of *Drosophila pseudoobscura*. *Genetics* **31**: 125-156.
- WRIGHT, S., TH. DOBZHANSKY, and W. HOVANITZ, 1942, Genetics of natural populations. VII. Allelism of lethals in the third chromosome of *Drosophila pseudoobscura*. *Genetics* **27**: 363-394.

ABSTRACTS OF PAPERS PRESENTED AT THE 1948
MEETINGS OF THE GENETICS SOCIETY
OF AMERICA

WASHINGTON, D. C., SEPTEMBER 11-13 1948

M. R. IRWIN, *Secretary*
Department of Genetics
University of Wisconsin
Madison, Wisconsin

AVERY, A. G., and A. F. BLAKESLEE, Smith College, Northampton, Mass.: *Effect of extra chromosomes on shape of stigma of Datura stramonium.*—The presence of specific extra chromosomes in $2n+1$ types of *Datura stramonium* has profound effects upon the morphology and physiology of plants affected due to unbalance exerted by genes in the supernumerary chromosome. Some parts of the plants are more visibly affected than others. There is little difference between the various types in respect to size and shape of anthers. There are great differences, however, as earlier pointed out, in form of leaf, capsule, adult and seedling habits of growth and anatomical structure of flower stalk such that the particular $2m+1$ type may usually be identified by one of the above characters alone. To the above list of diagnostic characters we are now able to add form of stigma. Photographs will be shown to illustrate stigma forms induced by extra chromosomes such as the flat-topped stigma of the $2n+11\cdot11$, the narrow dark purple stigma of $2n+23\cdot24$, the enlarged stigma of $2n+9\cdot10$, the more or less spherical stigma of $21\cdot22$, etc. The forms of stigmas of the secondary (II) $2n+1$ types show a similar relationship to their related primaries as is shown by other morphological characters described earlier. The wide range of changes in different parts of the plant brought about by single extra chromosomes emphasizes the interaction of chromosomes and their constituent genes in control of the processes of growth and differentiation.

BAKER, WILLIAM K., University of Tennessee, Knoxville, Tenn.: *The production of chromosome interchanges in Drosophila virilis.*—Males of *D. virilis* were treated with X-ray dosages of 1000, 2000, 3000, and 4000 r units. Any translocations induced in the sperm of these males between chromosomes 2, 3, 4, 5, and Y were detected by a conventional genetic analysis. In strictly comparable experiments, the temperature at the time of irradiation was maintained at either 3° or 28°C. A significantly greater number of translocations are produced at the lower temperature. The results of the cold series, in regard to both the percent of translocations induced and the minimum number of induced breaks, agree very closely at all dosage levels with the mathematical expectations based on the following main assumptions: (1) the number of breaks per sperm follows the Poisson distribution (2) each of the major autosomes is equally likely to be broken, (3) the mean number of breaks increases linearly with dosage, and (4) the broken chromosome ends unite independently and at random. The decrease in the number of interchanges produced at the

warm temperature cannot be attributed to an alteration in the process of joining of the broken ends since the relative numbers of translocations involving two, three, or four chromosomes in both the warm and the cold temperature experiments agree with the expectation. It appears, therefore, that this differential effect is caused by a direct or indirect action of heat on the breakage of the chromosome thread.

BELL, A. E., Iowa State College, Ames, Iowa: *Physiological factors associated with genetic resistance to fowl typhoid*.—Body temperature and phagocytic activity of polymorphonuclear leucocytes were studied in strains of chicks genetically differentiated in their resistance to fowl typhoid, *Shigella gallinarum*. Resistant chicks consistently evidenced normal temperatures 0.2° to 0.4°C higher than chicks of the susceptible strain. In inoculated groups the resistant strains maintained a higher temperature for a period of three to four days. Thereafter, susceptible chicks developed a significant fever temperature exceeding that of resistant individuals by one to two degrees C. Both within and between strain comparisons indicated that high body temperature and resistance were closely associated during the disease incubation period, but in the later stages of the disease fever temperatures were correlated with susceptibility. Phagocytosis studies *in vitro* revealed equal phagocytic abilities for polymorphonuclear leucocytes from resistant and susceptible strains. Both strains showed greater phagocytosis with increasing temperature. Intracellular digestion of phagocytosed bacteria was negligible in polymorphs from the susceptible strain; however, marked lysis of bacteria was evidenced in resistant cells. This qualitative difference in intracellular digestive enzymes appears to be a major factor in genetic resistance to fowl typhoid. Higher body temperature during the early disease stages could be of some significance by enhancing phagocytosis and other defense mechanisms.

BOWDEN, WRAY M., Central Experimental Farm, Ottawa, Canada: *Cytogenetic studies on a trispecies Lobelia hybrid and its colchicine-induced tetraploid derivatives*.—A diploid ($2n=14$) trispecies hybrid was obtained by crossing *Lobelia fulgens* var. Queen Victoria Hort. with an artificial F_1 hybrid (*L. siphilitica* L. \times *L. cardinalis* L.). The hybrid was propagated vegetatively and during the most active growth phase, colchicine treatments induced myxiploidy. One of the vegetative descendants was completely tetraploid. The color of the corolla of the diploid (rose red to tyrian rose) was less intense in the greenhouse than that of the tetraploid (crimson to rose red). The tetraploid flower parts were larger than those of the diploid. The diploid hybrid was almost completely self-sterile; the capsules had a few light-weight seeds. The tetraploid was self-fertile and the large capsules had numerous well-formed seeds. The diploid hybrid had 27 percent normal pollen; the colchicine-induced tetraploid had 76 percent; and the seedlings were variable, for example, 88 percent, 80 percent, 62 percent and 41 percent. The tetraploids had a greater leaf area due to a marked increase in leaf width. The diploid hybrid was backcrossed to *L. siphilitica* and to *L. cardinalis*. The backcross hybrids showed a dominance

of the characteristics of the respective species parents but all seedlings had some characteristics of the Queen Victoria ancestor. Meiosis was more regular in the tetraploid trispecies hybrid and in the diploid backcross hybrids than in the diploid trispecies hybrid.

BRILES, W. E., and W. H. MCGIBBON, University of Wisconsin, Madison, Wis.: *Heterozygosity of inbred lines of chickens at two loci effecting cellular antigens.*—Evidence has been obtained indicating that two inbred lines of S. C. White Leghorns are heterozygous at two antigen determining loci. The birds tested were from Lines 1 and 2 developed at the REGIONAL POULTRY RESEARCH LABORATORY of East Lansing, Michigan. The lines have coefficients of inbreeding of at least 52 and 60 percent respectively. The individuals of each line were tested with two classes of serological reagents, which were developed by making use of random bred birds of known antigenic constitution. One class of reagents has been found to react with red cell antigens determined by genes at a single locus, given the designation *B* (Genetics 33: 97). The second class of serological reagents has proven specific for antigens determined by genes at a second independent locus, called *D*. Heterozygosity at both of these loci is indicated for the two inbred lines by the positive and negative cell agglutination reactions obtained with some of these reagents; that is, the cells of certain individuals were positive while others in the same line were negative with the same reagent. If the loci in question can be considered as representative, then general residual heterozygosity is indicated for both inbred lines. On the other hand, should there be some positive selective differential for heterozygosity at these antigen determining loci then the lines might still be relatively homozygous.

BURNHAM, C. R., University of Minnesota, St. Paul, Minnesota, and California Institute of Technology, Pasadena, California: *Chromosome segregation in translocations involving chromosome 6 in maize.*—In plants heterozygous for translocations involving chromosome 6 in which the interstitial segments were short (eight with the break in the long, three in the short arm of 6), adjacent 2 segregations ranged from 14 to 33 percent. In all but one of those in which one or both interstitial segments were long (seven in the long, one in the short arm of 6), adjacent 2 segregations were very low (0.2 to 7.6 percent). If a species with a single ring of four chromosomes had completely directed or alternate segregation, only in those with genetically short interstitial segments should spore abortion be low or absent. Sterility might be expected to reach a maximum of 50 percent as the length of this segment increased.

CASPARI, ERNST, and JOSEPHINE RICHARDS, Carnegie Institution of Washington, Cold Spring Harbor, N. Y.: *Differences in protein constitution of a^+a^+ and aa Ephestia.*—The gene *a* in Ephestia inhibits the transformation of tryptophane to kynurenin. The non-oxidized tryptophane is retained and stored at least in part in the proteins. Since the protein-N content is not increased, a qualitative difference in the cell proteins must be assumed. Experi-

ments were made to determine whether or not this difference in tryptophane content is restricted to a particular protein fraction. Larval proteins were fractionated by precipitation with alcohol. Six fractions were obtained in this way, a seventh being added by extraction with $n/20$ Na_2CO_3 . Increases in tryptophane content of *aa* larvae were obtained in four fractions, while the remaining three fractions gave equal percentages of tryptophane for both strains. The result does not permit one to decide the question. Differences were found in the rate of autolysis of a^+a^+ and *aa* tissue. Homogenates from a^+a^+ and *aa* larvae identical for the majority of the other genes were kept at 31°C and examined at intervals of non-protein nitrogen and non-protein tryptophane. The release of non-protein nitrogen and tryptophane was consistently faster in a^+a^+ material. It cannot be decided whether this result is due to an increased resistance of *aa* proteins against the proteolytic enzymes, or whether the proteolytic enzymes themselves are changed quantitatively or qualitatively under the influence of the gene *a*. In either case, a difference in protein constitution between the two strains would be confirmed.

CLANCY, C. W., University of Oregon, Eugene, Oregon: *Comparative measurements of eye color pigment in Drosophila melanogaster*.—The amount of pigment contained in extracts of the heads of wild type and the mutant eye color stocks, *v*, *cn*, *st*, *cd*, *v;cn*, *v;st*, and *v;cd* has been determined colorimetrically. Statistical analysis of the data indicates that significant differences in pigment content exist between each of these stocks except in the case of *cn* versus *cd*. The order, from lowest to highest in content of "red" pigment, is $v \rightarrow st \rightarrow v;st \rightarrow v;cn \rightarrow v;cd \rightarrow (cn \text{ and } cd) \rightarrow \text{Ore-Rc}$, with a difference of approximately 25 percent between vermilion and cinnabar.

Colorimetric determinations of the relative amount of pigment contained in extracts of the heads of vermilion flies heterozygous for various alleles of the white gene, and of their control vermilion sibs have been made. In all cases studied the heterozygotes have less eye pigment (red component) than their control sibs. Moreover, a curious but statistically significant pairing occurs such that for the alleles considered, and under the conditions of the experiments, the order from lowest to highest in content of "red" pigment, and the pairing is as follows: w^a and $w^t \rightarrow w$ and $w^e \rightarrow w^{co}$ and $w^h \rightarrow w^{bl}$ and w^{nat} .

CLANCY, C. W., and W. S. WELBORN, University of Oregon, Eugene, Oregon: *Ovary transplants in Drosophila melanogaster: location of factors affecting fertility of lozenge females*.—Wild type females into which ovaries of the relatively infertile mutant, *lozenge*^{34k} were implanted produced significantly more lozenge offspring when test-mated than did unoperated lozenge females. This result is in agreement with inferences based on the work of C. P. OLIVER, R. C. ANDERSON, and M. M. GREEN (1941-1945) indicating that the relative infertility of lozenge females is due, in part, to factors residing in the genital duct and/or accessory organs rather than in the gonads.

CLARK, A. M., and C. J. MITCHELL, University of Delaware, Newark, Del.: *Dosage relations of haploids and diploids for the mutant stubby of Habro-*

bracon.—Comparison of haploid males (C +, C sb), diploid males (C +/+ sb, C sb/+ sb) and diploid females (C +/+ sb, C sb/+ sb) for the mutant stubby (sb) (antennal shortening and segmental disarticulation with tendency toward segmental fusion) shows that the dosage effects upon the diploid males are greater than upon either the haploid males or females. Heterozygous stubby females are phenotypically wild-type while the heterozygous stubby diploid males show incomplete dominance of the wild-type gene over its stubby allele. Counts of wing microchaetae indicate that diploid males have larger cells than either the haploid males or the females. It is suggested that the degree of dosage effect of the gene stubby is related to cell size which in turn may be influenced by the rate of cell division.

CONGER, ALAN, D., Oak Ridge National Laboratory, Oak Ridge, Tenn.: *The cytogenetic effect of sonic energy applied simultaneously with X-rays*.—An experiment has been performed to test the influence of sonic energy on the yield of X-ray induced chromosomal aberrations in a clone of *Tradescantia paludosa*. Chromosomal aberration frequency was determined at the microspore mitosis from acetocarmine smears made 4 days after treatment.

Inflorescences were immersed in water contained in a steel cup used for the sonic treatment. The bottom of the cup was a vibrating diaphragm which transmitted the sonic energy to the plant buds via the water. The instrument used was a Raytheon Mfg. Co. magnetostriction oscillator, run at 9,100 cycles/sec and at a power of 30 watts. Two treatments were given to inflorescences inside the sonic cup: a) 250 r X-rays (78 r/min) as measured in air outside the cup, and b) 250 r X-rays (as above) plus sonic treatment begun with and continued for five minutes after the X-radiation ceased.

The frequency of all types of chromosome aberrations was higher when the sonic treatment was given in addition to the X-rays. The ratio of X-ray plus sonic energy/X-ray aberrations was 1.3/1 for both exchanges and simple deletions. The sonic treatment alone, as given here, did not cause aberrations.

This increased yield of aberrations is probably due to an increased amount of chromosome movement caused by the transmission of sonic energy through the cells during and after the X-radiation; movement would separate the broken ends from a single chromosome break (reducing restitution) and bring together broken ends from different breaks (increasing new reunions)—both would increase aberration frequency.

COTTERMAN, C. W., University of Michigan, Ann Arbor, Mich.: *Status Bonnevie-Ullrich*.—BAGG and LITTLE described an inherited syndrome in the mouse, consisting of defects of the eyes, eyelids, feet, and other parts, commonly occurring unilaterally and in varying combination. This complex, called myelencephalic blebs (*Mb*), owes its name to embryological studies of BONNEVIE, who showed that excessive exudation of cerebrospinal fluid from the primitive fourth ventricle leads to formation of large skin blebs in the neck region, which migrate into concavities of the embryo's surface and into limb buds, causing abnormal development of underlying structures. ULLRICH

(1936) showed that a rare human anomaly, pterygium colli, a bilateral wing-like fold of neck skin, was usually associated with defects similar to those of *Mb* mice, and probably of similar origin. "Status Bonnevie-Ullrich" is discussed in the German and Swiss literature. The case reported here is typical. A girl, aged 5, showed at birth: pterygium colli, strabismus, epicanthus, abnormal ears, bowed upper lip, edematous hands and feet, cutis laxa, hypoplasia of nipples, coccygeal fistula, left clubfoot, accelerated ossification, slight dwarfism, simian palm crease, peculiarities of palmar dermatoglyphics. Near relatives show none of these defects, excepting strabismus and epicanthus, conspicuous in a brother, mother, and maternal cousin. ULLRICH emphasized that the bleb fluid first overlies the brain stem where it might damage cranial nerve ganglia, so that strabismus and other facial paralyses might be expected as minimal manifestations. Thus interpreted, the present family would seem to support ULLRICH's theory and suggest variable dominant inheritance.

COTTERMAN, C. W., H. F. FALLS, and J. V. NEEL, University of Michigan, Ann Arbor, Mich.: *Some hereditary diseases having subclinical manifestations in carriers.*—The development of techniques for the detection of genetic carriers of inherited disease is both theoretically significant and practically important. For present purposes a "carrier state" may be defined as arising under the following genetic situations: (1) an autosomal gene producing a severe disease in homozygotes, has mild effects in heterozygotes; (2) a sex-linked gene producing a pathological effect in males has minor, subclinical effects in heterozygous women; (3) an autosomal gene producing disease symptoms in some heterozygotes has only minor, non-pathological manifestations in other heterozygotes. Under (3) we may include carrier states recognized in individuals of different sex or of earlier age than those who show disease symptoms. Studies carried out at the UNIVERSITY OF MICHIGAN HEREDITY CLINIC during the past several years provide materials for illustrating the above conditions. Six hereditary diseases have been selected for purposes of demonstration: (a) thalassemia major (Mediterranean anemia); (b) xanthoma tuberosum and hypercholesterolemia; (c) Ehlers-Danlos syndrome, a defect of the elastic connective tissue; (d) sex-linked anemia; (e) sex-linked choroidoretinal degeneration; and (f) gout and hyperuricemia.

DUNCAN, ROBERT, E., and J. G. ROSS, University of Wisconsin, Madison, Wisconsin: *Nuclei of maize endosperm.*—The nuclei in maize endosperm increase vastly in volume and surface area up through the "milk" stage. The chromosome number remains constant at 30 during this increase as determined directly during endomitosis and indirectly in energetic nuclei by (1) number of knobs and (2) of heterochromatic bodies on the surface of the nucleolus. Using knobs to delimit portions of chromosomes, determinations of the number of strands per chromosome can be made after enlargement of the nucleus. They are polytene. The nuclei are smaller near the embryo, which suggests a possible relationship between its development and nuclear growth in the endosperm. There is also a relation between polyteny and the storage function of the endosperm.

EVERETT, H. L., Connecticut Agricultural Experimental Station, New Haven, Conn.: *Normal and abnormal chloroplast production in Zea mays*.—Normal production of plastids and plastid pigments is associated with a relatively dark yellow endosperm color in the maize inbred designated 1164, while light endosperm color is associated with lethal chlorophyll deficiencies in this inbred. Crosses of 1164 with a normal green inbred (A158) were made and selfed. Segregating F₂ and F₃ generations were selected for chloroplast production under constant temperature conditions. Chloroplast formation ranged from pseudo-normal to complete albinism in seedlings correlated with light endosperm kernels. In this material at least two genes are involved in chloroplast formation. One, completely dominant and correlated directly to endosperm color, yields normal plants in homozygous and heterozygous state. The other gene which is hypostatic and detectable only in plants grown from light endosperm kernels, yields pseudonormal green seedlings in the homozygous dominant condition, yellow-green seedlings in the heterozygous state, and completely albino seedlings in the homozygous recessive state. These seedling types are not viable under field conditions, but dark endosperm kernels which yield normal plants under field conditions can be selected so that the normal gene is associated with the hypostatic supplementary gene either in the homozygous dominant, heterozygous or homozygous recessive condition. Field trials indicate that seedlings with the normal gene associated with the hypostatic dominant gene are initially favored over seedlings of the normal gene associated with the homozygous recessive albino condition. These findings show that normal chlorophyll is formed by plants of different genetic composition for plastid production.

FABERGÉ, A. C., University of Missouri, Columbia, Missouri: *Chromosome aberrations in Tradescantia produced by X-ray treatment at liquid air temperature*.—A technique has been devised for freezing ripe *Tradescantia* pollen down to liquid air temperature, about -192°C . This pollen can be subsequently germinated on standard medium, and metaphase chromosomes observed at the division of the generative nucleus in the tube. Liquid air treatment by itself has no observable effect on subsequent division, which appears quite normal in every way. If X-ray treatment is applied to pollen while it is in liquid air, chromosome breaks and aberrations are produced which, qualitatively, do not seem to differ from those obtained by X-raying at room temperature. The number of breaks and aberrations is, however, several times less than would be the case at ordinary temperature, and to get a comparable frequency, a very much heavier X-ray dose has to be used. This decreased sensitivity is quite different from the effects within the physiological range of temperature observed in *Tradescantia* microspore divisions. In this range (about $+2^{\circ}\text{C}$ to $+35^{\circ}\text{C}$) more aberrations are produced at lower temperatures, as has been shown by several workers. It is hoped that this method, by eliminating chromosome movement and presumably also restitution, may simplify some of the problems of radiation cytology.

FOX, ALLEN S., University of Chicago, Chicago, Ill.: *Antigenic effects of certain single gene mutations in Drosophila melanogaster*.—An isogenic strain of *D. melanogaster* and two derived strains differing from the isogenic by X-ray induced mutations, one at the *v* locus and one at the *rb* locus, have been subjected to antigenic analysis by means of methods previously outlined (Fox, A. S., 1948, *Genetics*, **33**: 104). Anti-isogenic serum, when absorbed by vermilion antigens, still reacts strongly with isogenic antigens, but with neither vermilion nor ruby antigens. The same serum, when absorbed by antigens of the ruby strain, still reacts strongly with the isogenic antigens, reacts very weakly with vermilion antigens, and not at all with ruby antigens. Somewhat similarly, anti-vermilion serum, when absorbed by either isogenic or ruby antigens, still reacts strongly with vermilion antigens, but with neither isogenic nor ruby antigens. To date, however, anti-ruby serum, when absorbed by either isogenic or vermilion antigens, does not react with antigens of any of the three strains.

These results may be taken to indicate a more complex situation than would be expected on the hypothesis of a one to one relationship between gene and antigen. At least the *rb* and *v* loci seem to be involved in the production of an antigen or antigenic complex by means of interaction.

FRASER, F. C., and M. L. HERER, McGill University, Montreal, Canada: "*Lens rupture*": a new recessive gene in the mouse.—The morphological effects of a mutant character inherited as a simple recessive factor in the house mouse will be demonstrated. The condition is characterized by the appearance, at about five weeks of age, of white opaque areas in the eyes of affected mice. This is shown to be associated with a degenerative process in the lens involving expulsion of the lens nucleus into the vitreous chamber of the eye and sometimes the passage of the shrunken, distorted lens into the anterior chamber.

GALINSKY, IRVING, University of Wisconsin, Madison, Wisconsin: *The effect of certain phosphates on mitosis*.—The treatment of *Allium cepa* roots with Na_2HPO_4 , NaH_2PO_4 , and K_2HPO_4 causes certain departures from normal mitosis which resemble those resulting from mitotic poisons such as colchicine, etc. in some respects, and from sodium nucleate in others. The intensity of the effect is greatly influenced by the concentration and duration of treatment.

The following phenomena have been observed as a result of phosphate treatment: large nuclei, nuclei with large Feulgen-positive regions, sticky chromosomes, lampbrush chromosomes, nucleoli with Feulgen-positive bodies, lagging chromosomes, non-disjunction, abnormalities in chromosome size, one or more chromosomes lying off the equatorial plate, chromosome clumping, premature visible-splitting of chromosomes, fragmentation, dumbbell-shaped nuclei, binucleate and multinucleate cells, polyploid cells, giant cells, delay in spindle formation, irregular chromosome segregation, upset in nucleic acid distribution, failure of nuclear membrane to increase in size and delay in its breakdown until metaphase, increase in density of cytoplasm.

The above phenomena are remarkably similar to those found in many tumor tissues which suggests that an upset in phosphate metabolism may be the cause of abnormal mitoses found in some tumors. This is supported by the findings of many workers that a number of tumors show an increase in phosphatase activity.

GOWEN, JOHN W., Iowa State College, Ames, Iowa: *Genetic differences in radiation effects on resistance of mice to typhoid, Salmonella typhimurium.*—Six of our inbred strains of mice are differentiated in their numbers of leucocytes: S 19.6, R.I. 22.5, Z 16.1, E 14.6, L 11.6, and Ba 11.1 thousands per cmm of blood. The resistance of these strains to mouse typhoid, as demonstrated by injections of 200,000 bacteria of line 11c *Salmonella typhimurium*, is highly correlated with the strain's leucocyte number. Exposing a strain to X-rays decreases the strain's resistance, the amount of the decrease following the relation, $\text{survival} = ae^{-kd}$ where d is dose in r units. The strains differ in their initial numbers of leucocytes (a) but not in their slope constants (k). Examination of the numbers of leucocytes after various roentgen doses of X-rays shows that the numbers of leucocytes are depressed exponentially in each strain. This fact explains the observed effects of X-rays on resistance and adds significance to the genetic influence which regulates the numbers of leucocytes. Under the same dose of X-ray some strains die and other live, but this is not due to a differential action of irradiation but to the genetic background controlling cellular reproduction.

HAPP, G. B., The Principia College, Elsah, Ill.: *Some considerations of trends in genetics.*—The current studies in psychobiology in which biological entities are viewed broadly as conjunctively mental and physical also contribute to a broader view of the gene. In this broader view, the gene, too, may be considered a joint psychobiological entity physically evidenced in the chromosomal structure and conjunctively existent in a habit or pattern.

It has long been recognized in ecology that various stages of relations such as cooperation and competition exist between biological entities. These stages of relations may also exist between genes. For instance, the stage of uneven competition appears to be present in the occurrence of dominant-recessive relations in genetics.

Consideration is being given to these general psychobiological states and ecological relations found in general biology and possibly in certain instances in genetics. They warrant further consideration, investigation, and verification in solid factual demonstrations.

HERSKOWITZ, IRWIN H., Louisiana State University, New Orleans, Louisiana: *Hexaptera, a homoeotic mutant in Drosophila melanogaster.*—Several homoeotic mutants have been discovered in *Drosophila melanogaster* which result in replacement of certain organs of the normal fly by parts resembling other organs. Hexaptera is a spontaneous, homozygous viable, dominant mutant located on chromosome 2. Its action results in the formation of appen-

dages, frequently bilateral, on the dorsal part of the prothorax. Hexaptera is a homoeotic mutant in the sense that the appendages produced may take different forms, such as wing, haltere, or leg. The region of attachment of these appendages to the dorsal prothorax is the same for all types, and cases of three or four supernumerary appendages in this region are not uncommon. Penetrance is variable and is dependant on both genetic and environmental factors. Genetic modifiers of penetrance are distributed throughout the chromosome complement. Penetrance improves in densely populated cultures and is greater at 25°C (6.5 percent in ♂♂ and 24.2 percent in ♀♀) than at 20°C (1.5 percent in ♂♂ and 3.3 percent in ♀♀).

A working hypothesis is proposed that Hexaptera causes a dorsal prothoracic anlage to grow and that the type of appendage which it forms may be determined in the same manner as it is in other homoeotic mutants.

HINTON, TAYLOR, Amherst College, Amherst, Massachusetts: *Analysis of chromosomal rearrangements affecting the expression of a position-effect.*—A cytological study of a series of chromosomal rearrangements in *Drosophila melanogaster* has been undertaken. The effect of these rearrangements on the phenotypic expression of the position effect associated with Inversion (2LR) 40d has been noted. The phenotype caused by this inversion is not altered by any rearrangements except those having a break in common with at least one of the breaks of the inversion. The phenotype may be altered by rearranging either end of the original inversion. It appears that the position of heterochromatin is the principal factor affecting the phenotype.

HOLLANDER, W. F., Yale University School of Medicine, New Haven, Conn.: *Some observations on placental fusions in mice.*—Among 570 pregnant mice examined at autopsy 35, or 6 percent had a pair of embryos with a common placenta or attached placentas. The pregnancies had been chosen at random among several strains, and the placental fusions were found in almost every genetic group. Age of the mother and season of the year seem to have had little influence on the occurrence of fusions, since the mothers were from two to thirteen months old, and were killed in every month of the year. There is a marked tendency for the cases of fusion to occur in the more crowded uterine horn, but crowding is not necessary as in one instance the only two embryos in a horn, and in several instances two of three in a horn, showed attachment. Identical twinning seems unlikely since the joined embryos are often heterosexual, as found by CARR, and in three instances they have differed in genetic eye color.

HOROWITZ, N. H., California Institute of Technology, Pasadena, Calif.: *The one gene-one enzyme hypothesis.*—It has been suggested that the preponderance of single-functioned genes among biochemical mutants of *Neurospora* is the result of selection in detecting mutations. Mutations of multiple-functioned genes, it is argued, are selected against, since mutation of these genes will usually involve loss of reaction products which, because of their non-

diffusibility, or for other reasons, cannot be restored from the outside (see DELBRÜCK's discussion following paper by BONNER in Cold Spring Harbor Symposia on Quantitative Biology, 11).

A means for determining the relative frequency of "irreparable" mutations based on temperature mutants, has been devised. Temperature mutants are phenotypically normal in one temperature range and mutant in another. Two classes exist: (a) those which grow on minimal medium at one temperature but which require some component of complete medium at other temperatures, and (b) those which grow on minimal at one temperature, but which fail to grow on either minimal or complete at other temperatures. It is suggested that the relative frequency of these two classes is equal to the relative frequency of reparable and irreparable biochemical mutations in *Neurospora*. Assuming a random distribution of functions among genes, it is then possible to derive an expression which permits a calculation, from experimental data, of the frequency of genes with a single function. Calculations based on present data indicate a value of at least 0.74 for this frequency. Because the number of temperature mutants on which this estimate is based is small, and for other reasons, this figure is to be regarded as a rough approximation.

HUESTIS, R. R., University of Oregon, Eugene, Ore.: *Red eyed Peromyscus maniculatus*.—An interesting gene substitution has been found in *Peromyscus* which produces a reduction of pigment in one or both eyes, but has no observable effect upon the pelage color. The eye color overlaps but averages darker than that of pink eye. Test cross matings of black eyed heterozygous mice with mice having both eyes red have produced 105 young; 52 percent of which had black eyes, 24 percent one red eye and 24 percent both eyes red. 17 of the odd eyed mice had the red eye on the right side. Smaller series of young from other matings have shown that red eyed parents throw some black eyed young and that parents with but one red eye throw a significantly higher ratio of black eyed young than parents with both eyes red.

HUSKINS, C. LEONARD, University of Wisconsin, Madison, Wisconsin: *Experimentally produced somatic reduction and segregation*.—Reduction divisions occur naturally in somatic tissues of plants and animals much more commonly than has been recognized. Increasing the concentration of various substances normally present in the cell increases their frequency. The most effective agent yet found for plants is sodium nucleate (see GALINSKY for effect of phosphates). Genetic evidence of gene and chromosome segregation induced by sodium nucleate has been obtained with heterozygous tomatoes and monosomic wheat respectively. Cytologically the induced reduction divisions range from near the type characteristic of normal meiosis in the plant treated to types described previously in protozoa, *Sciara* and coccids. They therefore afford an opportunity to evaluate the factors involved in meiosis and suggest that several features commonly considered essential to segregation may be secondary adaptations.

The most abundant evidence of induced pairing is found in *Rhoeo*. In *Crocus* "distance-conjugation" occurs. Evidence that homologues segregate in greater than random frequency without previous pairing has been obtained in *Trillium*. A complex orchid hybrid has given proof that neither gonometry or segregation of the genome as a unit occurs. In the onion all types have been found from reduction following pairing with and without chiasmata to segregation at prophase without pairing or spindle formation. Haploid cells occur but most common is segregation, without prior pairing, followed immediately by restoration of the diploid number, through an abortive second division. Chromosome pairing occurs in the diploid pollen of tetraploid *Tradescantia*, adding to previous evidence of double reduction in polyploids.

ILTIS, HUGO, Mendel Museum, Fredericksburg, Virginia: *On the inheritance of lacking incisors*.—Two cases of lacking upper lateral incisors and two pedigrees showing their inheritance are described. The first case showed four instances of lacking incisors in two generations, the second nine instances in two generations. In the first case there were two instances, in the second case there were three instances where neither of the parents of the afflicted persons showed the deficiency. From both pedigrees it can be concluded that the gene in question is, probably, a recessive one.—There are many cases of lacking incisors described in the literature but in none of them a recessive mode of inheritance has been reported. To the "dominant," "irregular dominant," and "sex-linked" cases of the literature our recessive cases are added. Instances of other abnormalities where a single variability in the mode of inheritance has been observed, are quoted. The problematic nature of our knowledge in regard to the mode of inheritance of many human characteristics is emphasized.

IVES, PHILIP T., Amherst College, Amherst, Mass.: *Seasonal shift in frequency of lethal chromosomes in the local wild population of *Drosophila melanogaster**.—Wild flies were collected in the summers of 1946 and 1947. One second chromosome of each fly was analyzed for the presence of a lethal or semilethal gene (less than 17 percent of homozygotes in the test generation). The following percentages of lethals and semilethals combined were found. In 1946: Aug., 48 tests, 27 percent; Sept., 21 tests, 43 percent; Oct., 58 tests, 52 percent. In 1947: July, 33 tests, 21 percent; Aug., 82 tests, 35.4 percent; Sept., 185 tests, 38.4 percent; Oct. 76 tests, 39.5 percent. The 1946 summer was comparatively late, cool and wet; 1947 was earlier, hot and dry. The similarly low percentage in the first collection of each summer seems too different from the other percentages to be accounted for by chance or by subsequent mutations in each summer. The lesser increases in the later collections in each summer can probably be accounted for by mutations and by chance. The Sept.-Oct. percentage in 1947 is significantly lower than that found in any of the similar collections in earlier years. The proportion of identical lethals, however, was not significantly higher in 1947. It seems possible that shifts in the proportion of lethals and semilethals both within and between years reflect environmental influences on the heterosis of many of the lethals together with changes in population size.

JEFFREY, E. C., Harvard University, Cambridge, Mass.: *Hormones in relation to parthenogenesis*.—Although the genera *Trillium* and *Tradescantia* have been used for many years in connection with the important subject of the organization of chromosomes in relation to cytogenetics, it has not been realized that most, if not all, species of these genera are parthenogenetic. The parthenogenesis is of a remarkable type, since the haploid eggs in both genera give rise to diploid embryos, which, although resulting from a normal reductional or meiotic division, are remarkable in the fact that they are not normally capable of fertilization. They assume the diploid condition not as the result of the normal fusion of the haploid male and female gametes but as the consequence of the action of hormones derived from the deposition of pollen on the stigmas of their flowers. The pollen grains produce abortive pollen tubes, into which the typical two nuclei either do not pass at all or fail to reach the egg. In the young embryo, the transition from the haploid gametic condition to the diploid somatic state is effected by a double division of the chromosomes at metaphase. In younger embryos the transition may readily be seen but as these become older and larger, the divisions become entirely diploid. As a consequence of this curious cytological condition, diploid parthenogenesis results and the recognized relative constancy of that condition gives rise to a new species.

KAUFMANN, B. P., M. R. McDONALD, and H. GAY, Carnegie Institution of Washington, Cold Spring Harbor, N. Y.: *The ribonucleic acid content of chromosomes*.—The presence of ribonucleic acid in plant and animal chromosomes has been determined histochemically by utilizing crystalline ribonuclease (freed of proteolytic activity) in combination with various staining methods. It has also been demonstrated that the ribonucleic acid may be present in more than one form, and that the manner in which it is combined affects its stainability. For example, the safranin-gentian violet-orange G combination when used on Flemming-fixed root-tip sections permits a pattern of differentiation in which metaphase and anaphase chromosomes are colored red, those of late telophase and early prophase violet. Ribonuclease hydrolyzes the red-staining component, so that the condensed chromosomes color violet after exposure to the enzyme; more extended treatment will also impair stainability with gentian violet. These observations indicate that in addition to a constant ribonucleic acid component of the chromonematic threads, there is a more labile chromosomal ribonucleic acid that undergoes a cycle of accretion and dispersion in the course of mitosis coincident with the disappearance and reappearance of the nucleolus. It is suggested, therefore, that the accumulation of ribonucleic acid provides a state of "temporary heterochromatization" during metaphase and anaphase which presumably serves to inhibit genic activity. Ribonucleic acid is also a major component of permanent heterochromatin; for example, it has been identified in proximal and intercalary regions of the salivary-gland chromosomes.

These experiments, moreover, have shown that ribonucleoprotein can be degraded by ribonuclease which releases a pepsin-digestible protein stainable with acidic dyes.

KIMBALL, R. F., Oak Ridge National Laboratory, Oak Ridge, Tenn.: *The induction and inheritance of mutations in Paramecium aurelia*.—Beta radiation up to 13,000 r.e.p. has no immediate effects on stock 90 of variety 1 of *Paramecium aurelia*. When the descendants of rayed animals are sent through autogamy to make them homozygous, many are of reduced vigor. Evidence from inheritance studies indicates that the reduced vigor results from segregation into homozygous form of mutational changes induced in the micronuclei. Doses given in small daily fractions were just as effective as those given at a single exposure. Thus two-hit chromosomal aberrations could not have made a major contribution to the effect. However, the relation of the average fraction of exautogamous clones of reduced vigor to dose showed that a multiple hit phenomenon was involved. This is interpreted to mean that the majority of the effect is due to the combined action of mutant genes which are individually undetectable. A formula was developed relating the average fraction of reduced vigor to the mean number of mutations per micronucleus. The formula gives results consistent with the expectation that animals resulting from a cross of rayed to non-rayed should have on the average half as many mutants per micronucleus as the original rayed animals. From the formula, it was calculated that approximately two mutations per micronucleus were induced per 1,000 r.e.p. This rate is quite high and suggests that the method can detect mutations in the great majority of all loci in *Paramecium*.

KING, E. L., and E. F. PADDOCK, Ohio State University, Columbus, Ohio: *Triploidy in Rhoeo discolor Hance*.—The triploid condition ($3n=18$) has been demonstrated in both PMC and root tips of a clone. It is presumed that the original plant arose when an unreduced gamete was fertilized by a normal gamete. Fifty PMC at MI were analyzed. A mean of 0.66 ± 0.01 half chiasmata per chromosome was calculated. Univalents were present in 98 percent of these PMCs, with a mean frequency of 2.88 ± 0.21 univalents per PMC. The ring bivalent sort of association was seen in 64 percent. Three-arm associations were found in 82 percent. No 4-arm associations were seen. The largest single configuration included 14 chromosomes, of which 11 were in a continuous catenated chain. Configurations with more than 6 chromosomes were found in 28 percent. Within configurations ring bivalents were never adjacent. They always had at least one chromosome between them in the chain. The hypothesis of origin is consistent with all these data. Of the theoretically possible configurations, all involving five or fewer chromosomes were seen. In one of the PMCs studied, fragmentation had occurred, producing two half chromosome fragments.

KITZMILLER, JAMES B., University of Illinois, Urbana, Illinois: *Time relationships in the development of aphid wings*.—The development of wings in aphids offers a good opportunity for the study of gene action. The chrysanthemum aphid, *Macrosiphum sanborni*, is normally wingless, but can be induced to produce wings under the influence of continuous electric light and low (18°C) temperature. No males are known in this species; all individuals are

parthenogenetic females. A line descended from a single female, therefore, is of nearly uniform genotype.

In winged aphids the wings are determined a considerable time before wing buds appear. A measurement of the time interval between these processes of determination and differentiation affords one approach to the study of the process of development.

The time of embryonic determination of wings and the time of visible differentiation of wings were both calculated in a stock of aphids descended from a single female. The time of determination was found to be 3.27 days before birth. The time of visible differentiation (initial thickening of the hypodermis) was found to be 1.25 days before birth. The time interval between determination and differentiation, therefore, is approximately two days.

In another species belonging to the same genus, the corresponding time interval is only twelve hours. These results indicate that whatever is causing wing differentiation in the chrysanthemum aphid takes a relatively long time to act. The process of differentiation could be a very slow one, or perhaps one in which many steps are involved.

LEDERBERG, ESTHER M., University of Wisconsin, Madison, Wis.: *The mutability of several Lac^- mutants of *Escherichia coli*.*—Mutants of *E. coli* unable to ferment lactose have been secured as described in the next abstract. Some of these mutants (Lac^-) form colonies in which occur small, raised lactose-positive (Lac^+) areas. Independent occurrences of Lac^- mutants vary in their revertibility. A segregation for mutability was observed among the recombinant prototrophs obtained when an unstable Lac^- (Y-87) was crossed with a stable Lac^- strain (W-112). A Lac^+ papilla was isolated from each of 21 colonies of the most mutable strain, Y-87. Each was crossed with wild type Lac^+ . Of the 31,000 recombinants examined all but one were Lac^+ . Therefore, the change from Lac^- to Lac^+ is probably a reverse mutation. A similar study was initiated with the occasional papillae found in old colonies of the most stable strain, W-112. The strains isolated were slow fermenters (Lac^s), Lac^+ , Lac^s , and Lac^- recombinants were obtained from crosses with a suitable Lac^+ . The Lac^s cells from W-112 thus carry a "suppressor" gene. A second distinct suppressor leading to full fermentation of lactose has also been found. One slow fermenter isolated from irradiated cultures of Y-87 mutates rapidly to both Lac^+ and Lac^- . Further studies on the genetic determination of mutability are in progress.

LEDERBERG, JOSHUA, University of Wisconsin, Madison, Wis.: *Gene control of β -galactosidase in *Escherichia coli*.*—A large series of β -galactosidase mutants of *E. coli* was obtained by irradiating heavy cell suspensions on the indicator medium, EMB Lactose Agar. The mutants were compared phenotypically and genetically (see Genetics 32: 505). Most of the mutants involved the locus Lac_1 and were phenotypically alike (lactose⁻, methyl galactoside slow). Altogether, however, at least seven and probably ten distinct loci were found, mutation at any one of which leads to the loss or alteration of galactosidase.

Two of the mutant types have additional effects: Lac_6^- fails to split maltose or to ferment gluconic acid; Lac_3^- to split maltose or ferment glucose, galactosylase remaining intact. Several distinct mutations which partially "suppress" Lac_3^- have been found, leading to such phenotypes as $Lac^-Mal^+Glu^+$, $Lac^+Mal^-Glu^-$, and even $Lac^-Mal^+Glu^-$. While the latter suggests the direct or phosphorylative utilization of maltose, other evidence suggests that lactose is initially split by galactosidase. An allele of Lac_3^- has been found which is temperature-sensitive, showing different thresholds for the fermentation of sorbitol, of glucose or maltose, and the splitting of lactose, and pointing to the pleiotropic effect of the mutation. The complex gene-enzyme patterns suggest that some mutations have indirect effects on the production of one or more enzymes. It will be difficult, therefore, to point to a given gene as the source of specificity of a given enzyme, even though its mutation leads to the loss of that enzyme.

LONG, J. F., P. GERLAUGH, and D. C. RIFE, Ohio Agricultural Experiment Station, Wooster, Ohio, and Ohio State University, Columbus, Ohio: *A genetic study of gestation in cattle*.—The project from which the data for this study were collected was a cross-breeding project with cattle and was carried on at the OHIO AGRICULTURAL EXPERIMENT STATION. The experiment began in 1939 and will terminate in 1948. The breeding was conducted so as to produce four types of calves in approximately equal numbers each year: purebred Herefords; crossbreds (Angus sire-Hereford dam); purebred Angus; and crossbreds (Hereford sire-Angus dam). This routine was continued for the eight year period alternating the sires so that each cow would produce a purebred calf one year and a crossbred calf the next. The four types of calves were then compared. The 101 purebred Hereford calves were found to have an average gestation length of 286.3 days, while the average gestation period for the 99 purebred Angus calves was 276.4 days. This was a difference of nearly 10 days which was highly significant. The average gestation length of the crossbred calves was approximately halfway between the averages of the purebreds, being 283.2 days for the 102 calves produced by Angus sires and Hereford dams and 282.0 days for the 94 calves produced from Hereford sires and Angus dams. This was not a significant difference. A very high correlation was found between the lengths of gestation and the birth weights. This was significant or highly significant with all the four types of calves. Male calves were found to be carried 1.3 days longer than female calves, on the average and were 1.3 pounds heavier at birth.

LURIA, S. E., and R. DULBECCO, Indiana University, Bloomington, Ind.: *Lethal mutations, and inactivation of individual genetic determinants in bacteriophage*.—Transfers of genetic material among phage particles infecting the same cell are involved both in recombination of phenotypic characters and in production of active phage from particles carrying ultraviolet-induced lethal mutations. Experiments with particles carrying both lethal mutations and phenotypic markers were used to study the mechanism of transfer and the

relation between "loci" of phenotypic determinants and "units" in which lethal mutations occur. Bacteria were infected with one inactive irradiated particle $T2r^+$ and one inactive particle of the mutant $T2r$. A significant fraction of the bacteria yielded a mixture of active $T2r^+$ and $T2r$, which proved that the genetic transfers involved are not reciprocal exchanges occurring before multiplication. The failure of some bacteria to liberate one of the two types suggested inactivation (by lethal mutation) of the corresponding locus. The rate of this inactivation for a number of loci was studied by infecting bacteria with one particle of wild-type and one of a mutant, each particle carrying various numbers of lethal mutations. The presence or absence, in the yield from individual bacteria, of particles of each of the alternative phenotypes was determined, and from the frequency of the absence of each phenotype the inactivation of the corresponding locus was calculated. If, for example, the locus r^+ carries a lethal mutation, the bacterium will liberate no particle $T2r^+$. A first group of such tests will be presented, together with tests of the validity of assumptions made in using the results to measure the inactivation of single genetic determinants.

MARSHAK, A., New York University, New York, N. Y.: *The genetic significance of a nuclear precursor to desoxyribonucleic and ribonucleic acids.*—Isolated nuclei incubated at 37°C without added enzyme release nucleic acid but do not do so at 0° to 2°C. When the animal from which the nuclei are isolated is given P^{32} this nucleic acid has a specific activity 13 times greater than that of the RNA of the larger cytoplasmic particles (mitochondria) and 9 times greater than that of the smaller particles (microsomes). It is also greater than that of the phospholipids and the phosphate esters. Since the proportion of P^{32} held by the nucleus as compared with the rest of the cell remains practically constant from 2 hours to 5 days after administration, the high specific activity cannot be due to accumulation but to rapid turnover of the nucleic acid involved. The fraction extracted from the nucleus by methods for obtaining RNA has a specific activity approaching that of the nucleic acid in question and may therefore be similar or identical with it, but both differ from the RNA of the cytoplasm.

In both mitotic and non-mitotic cells the P^{32} appears first in this fraction. In mitotic cells it is subsequently accumulated in DNA while in non-mitotic cells it passes into the RNA of the cytoplasm. Because the nuclear nucleoprotein contributes to the formation of both the hitherto known nucleic acids by transferring constituents at least as complex as nucleic acids, and because it has properties in common with both, it is considered to be their precursor.

These findings indicate that plasmagens and other cytoplasmic constituents containing nucleic acid cannot be independent of nuclear activity. They also predict that cells will be found containing no DNA. A strain of bacteria with no DNA has been isolated. Asterias eggs show no detectible amounts of DNA in the meiotic stages and through the 2 cell stage of the embryo.

MARTIN, A. JR., J. N. DENT, and L. JOSEPH, University of Pittsburgh, Pittsburgh, Penna.: *Effects of beta-rays on Habrobracon juglandis.*—A technique

for exposing *Habrobracon juglandis* females to beta-rays has been developed and utilized. Wild-type females exposed to dried radioactive phosphorous produce abnormal progeny with a frequency of approximately 25 percent, while untreated females produce abnormalities at the rate of about 5 percent. Some of the abnormalities in the test material have proved to be mutations, while none of the abnormalities in the controls have been transmitted to their offspring. Frequency of abnormalities does not vary appreciably between progeny of treated virgins and non-virgins. Abnormalities occurring most frequently are those of the wings, antennae, and feet in that order. Mutations of wings and antennae have been checked through three generations. Reduplication of the right primary wing breeds true but with varying degrees of penetrance, even to the point of overlapping with wild-type. Wrinkled wings (primary and secondary) and drooping antennae appear in combination, indicating either a one-gene hit or a two-gene hit with genes so closely linked that they have so far shown no crossing-over. A clear-cut reduplication of the tarsal segments of the left mesothoracic leg has not bred true, but the abnormality indicates the severity of possible effects of beta-radiation. Current investigation indicates the need for extreme caution in the utilization of radioactive isotopes, particularly when used internally.

MITCHELL, CONSTANCE J., University of Delaware, Newark, Delaware: *Decrease in cell size associated with high diploid male viability in Habrobracon.*—Microchaetal counts were made for areas of 10,000 square micra in four regions of upper surface of right primary wing of *xa/xb* stock from mutation to high diploid male frequency (Dec. 1944). Averages were made in all cases for 100 specimens in each group reared from orange-eyed females crossed to wild type males. For standard temperature, 29°C, the median region averaged for diploid males, females, and haploid males respectively, 9.13, 12.23, 13.48; the radial region 12.75, 18.19, 19.81; the second discoidal 16.82, 21.20, 23.87; the third cubital 17.91, 23.32, 28.18. For 32°C culture temperature, averages were consistently lower for any given region and sex type; median 9.04, 11.86, 12.15; radial 11.93, 16.29, 17.18; second discoidal 16.02, 19.84, 21.99; third cubital 16.66, 21.09, 22.74. Relation of cell size for the three sex types is similar for a given temperature and wing region, being smallest in haploid males and largest in diploid males. Females are intermediate and, although diploid, approximate more closely their haploid than their diploid brothers. Counts have not previously been reported for wing regions other than the radial or for different temperatures. For radial region under standard conditions averages are higher, therefore cell size smaller, for this high diploid male stock than for any stocks previously reported. This is further evidence for association of diploid male viability with decrease in cell size.

MITCHELL, H. K., M. B. HOULAHAN, and J. LEIN, California Institute of Technology, Pasadena, California.: *Some aspects of genetic control of tryptophane metabolism in Neurospora.*—The development of a new method for selecting specific mutants of *Neurospora* has led to the discovery and investi-

gation of two new mutants concerned with tryptophane metabolism. One of these strains (C-83) will utilize tryptophane but not indole and consequently would be expected to lack an enzyme for catalyzing the coupling of indole and serine to give tryptophane. It has been found that such an enzyme system can be extracted from wild type *Neurospora* or from tryptophaneless mutants with a genetic constitution other than that of C-83. On the other hand, preparations from C-83 fail completely to effect *in vitro* synthesis of tryptophane.

The second new mutant found will utilize anthranilic acid, indole, tryptophane, kynurenine, 3-hydroxyanthranilic acid or nicotinic acid. A new link is thus provided in the complex problem of the over-all mechanism of tryptophane metabolism.

MITTLER, SIDNEY, Illinois Institute of Technology, Chicago, Illinois: *Genetic variation in populations of Drosophila melanogaster in the Chicago area.*—Wild *Drosophila* were trapped at various localities in Chicago and analyzed for second chromosome lethals and visible mutations. Second chromosome lethals varied in populations collected at one locality from 31.1 percent lethals of the total number of second chromosomes to 4.2 per cent. At another station in a collection of several hundred flies 57.1 percent of second chromosomes tested yielded lethals. In a collection two weeks later at the same locality only 20.2 percent of the second chromosomes tested had lethals. 20.3 percent of all second chromosomes tested contained lethals. Visible mutations were obtained by inbreeding of F_1 pair matings as described by SPENCER. There was a variation in frequency of number of mutations from station to station and a variation in visible mutant genes from the time of one collection to another. Several mutant genes were found in all collections.

MOREE, RAY, State College of Washington, Pullman, Wash.: *The bearing of hybrid sterility on the genetic relationship of Peromyscus t. truei and P. n. nasutus.*—Under field conditions both species may occupy the same habitat, but hybridization has not been observed (W. F. BLAIR, *Contr. Lab. Vert. Biol.*, **24**: 1-8, 1943; L. R. DICE, *Ecology*, **23**: 199-208, 1942). Under laboratory conditions an F_1 is produced consisting of fertile females and sterile males; the sex ratio is not unbalanced and the diploid number is 48 in both species. It has previously been shown that sterility is polygenic and results directly from deranged spermatogenesis (termination of spermatogenesis and/or production of abnormal sperm). As compared with intraspecific matings, interspecific matings result in a reduction of about 85 percent in litters per mating, 42 percent in young per litter, and 91 percent in young per mating; hence the reduction of productivity resulting from hybridization is due more to low production of litters than to reduction of litter size. Since the F_1 males are sterile, the F_1 females have a lowered fertility, laboratory hybridization is only 9 percent as productive as non-hybrid matings and natural hybridization has not been observed at all, it is clear that the two species are effectively isolated and that the isolation is genetic. While the genotypes of the two species ostensibly contain many genes in common, they differ with respect at least to some

of those genes which involve reproduction. To the extent that the experimental stocks are representative of the natural populations, results indicate that the likelihood of genotype alteration due to interspecific transfer of genes must be either very small or nonexistent.

NEEL, JAMES, V., University of Michigan, Ann Arbor, Michigan: *Ankylosing spondylitis in the K. kindred and the question of an "arthritic diathesis."*—Ankylosing spondylitis is a form of rheumatoid arthritis involving the vertebral column and the sacroiliac and hip joints, resulting in its end stages in a "poker spine." The evidence in the literature for the role of heredity in the etiology of the disease is not striking. In the K. kindred, a woman with ankylosing spondylitis had 13 children, three of whom have developed the condition, the diagnosis being based on physical examination, lumbosacral X-rays, and blood sedimentation rates. These three affected persons have five children, two of whom are likewise affected. The condition is thus transmitted in this kindred as if due to an autosomal dominant factor. Other forms of arthritis occurring in the kindred are: hypertrophic arthritis, menopausal arthralgia, and several complicated cases not fitting into any simple classification.—Certain clinicians have written of increased susceptibilities in some kindreds to disease of particular organ systems, the so-called "hereditary diathesis." This concept, because of sampling problems, is difficult to place on a sound statistical basis. But in kindreds such as the above, where there appears to be an arthritic diathesis, a logical explanation is provided by the postulate of the accumulation of a number of not entirely specific modifiers in a particular family, coincidental with or followed by the introduction of a genetic factor which ordinarily has a low penetrance, but which in the presence of these modifiers is well expressed.

OLIVER, C. P., University of Texas, Austin, Texas: *Individual and familial variations in anomalies of upper lateral incisor teeth.*—Among patients of a dental clinic, 427 or 4.8 percent had failed to develop one or more permanent teeth, excluding third molars. Complete oral radiographs were made of all persons lacking one or more of their teeth. Most frequently missing were second premolars and upper lateral incisors. In some families with several affected members, both the deciduous and permanent incisors failed to develop, in others only the permanent teeth were affected; in a few families, affected individuals differed in this respect. Variable expressions of the upper lateral incisor anomaly were observed in some individuals and in affected members of some families ranging from absence on both sides to presence on one and abnormal shape on the other side. Only 65 percent of *propositi* were bilaterally affected to the same degree; 18 percent were unilaterally affected; the others lacked a lateral incisor on one side but had an abnormally shaped tooth on the other side. Among affected relatives, the degree of manifestation also varied, but there was a definite tendency for relatives to be similarly affected. In approximately two-thirds of the families having affected parents and children, the degree of severity was identical in parent and all affected children. However, some lacking both upper lateral incisors produced children with

different degrees of severity of the trait. Other parents with a slight or unilateral expression produced children with the severest manifestation as well as children with lesser manifestations. Characteristic family histories and data on variable manifestations will be shown.

O'MARA, JOSEPH G., U. S. Department of Agriculture, University of Missouri, Columbia, Missouri: *Fertility in allopolyploids*.—The synthesis of the new allopolyploid combination *Triticum durum-Secale cereale* has made possible one direct test of the effect of chromosome number on fertility in allopolyploids. This amphidiploid has 42 somatic chromosomes, 28 of which come from *T. durum* and 14 from *S. cereale*. It can be compared with the amphidiploid involving *T. vulgare* and *S. cereale*, which has the same 42 somatic chromosomes plus 14 additional different ones. Available for comparison, therefore, are two amphidiploids; one with 42 chromosomes comprised of 14 chromosomes each of 3 different known genomes, A, B, and R; and the other with these same 3 genomes plus a fourth known as genome D. Both of these amphidiploids are partially asynaptic. Under identical conditions, the amphidiploid with 42 chromosomes was not more fertile than the one with 56 chromosomes. This comparison indicates that the hypothesis of KOSTOFF, that fertility in allopolyploids with large chromosomes is inversely related to chromosome number, can have exceptions. These observations may be explained by assuming (1) pairing anomalies peculiar to the strains involved or to the conditions of the experiment, (2) a specific antagonism between genomes A and B and genome R which is partially cancelled by genome D, or (3) that gametes of allopolyploids with high chromosome numbers can tolerate more aneuploidy than those with low numbers. Hypothesis 3 has some support from the fact that gametes of natural allopolyploids can tolerate more whole-chromosome deficiency than can the gametes of the known constituent species.

OWEN, RAY D., California Institute of Technology, Pasadena, Calif: *Antigenic characteristics of rat erythrocytes, and their use as markers for parabiotic exchange*.—Four cellular characteristics have been identified and utilized in this work. Two are controlled by allelic genes; the others are independent in inheritance. No linkage with other known loci has been established. The alleles may compete for a common substrate, since the heterozygote behaves as if it were intermediate in number of respective antigenic sites per cell. The four characteristics are first detectable at different ages, ranging from ten days (embryonic) to as long as fourteen weeks (postnatal). The two characters controlled by allelic genes do not appear at the same age. A very highly inbred strain of Wistar albino rat is heterogeneous for cellular characteristics. Each of the seven other inbred strains tested is homogeneous.—These erythrocyte differences provide convenient markers for an investigation of cellular exchange in parabiosis. Data have been collected covering such subjects as: time of first detectable exchange; extent of exchange; the approach to equilibrium of the two cell-types; the appearance of incompatibility and the course of auto-disjunction; the distribution of injected foreign cells; and time of persistence

of exchanged cells after surgical disjunction, a measure of the life-span of rat erythrocytes.

PAULEY, SCOTT S., Harvard University, Harvard Forest, Petersham, Mass.: *Sex and its relation to vigor in Populus*.—As an initial step in the study of natural variability within several native species of the genus *Populus* field collections were made at widely scattered points in the United States and Canada during the fall of 1947.

After assembly of the material the selected clones were sexed by dissecting the flower buds. Out of 76 clones bearing flower buds only 18 (23.7 percent) proved to be female. Since the criteria used in the selection involved such considerations as apparent health, vigor, good stem form, and lack of excessive branchiness the abnormal sex ratio suggests that a positive correlation may exist in this genus between maleness and these desirable economic characters.

A further ramification of more general biological significance is also suggested by these data: the vigor of the males may be directly traceable to the heterotic influence of an heteromorphic chromosome pair, *i.e.*, the XY mechanism which is claimed for *Populus* by at least two investigators. In most animals, such as man, where XY mechanism functions, it seems to be generally true that the heterozygous sex is more vigorous and larger though not necessarily of more desirable form. In the moths and butterflies on the other hand where the ZW sex mechanism prevails, in which the males are homozygous (ZZ) and the females are heterozygous for the sex chromosomes (ZW), the females are as a rule larger and more robust.

PHINNEY, BERNARD O., California Institute of Technology, Pasadena, California: *Cysteine mutants in Neurospora*.—Quantitative studies have been made of the growth requirements of mutant strains of *Neurospora* which are unable to synthesize the sulfur amino acid cysteine. These strains cannot grow on a minimal medium containing sulfate as the sole source of sulfur. One of these mutants, 35001, will grow equally well on the sulfonic acid cysteic acid and on the sulfinic acid cysteine sulfinic acid, as well as on cysteine; a second mutant, 80702, will grow on cysteine sulfinic acid and cysteine, but not on cysteic acid; and the third mutant, 86801, will grow only on cysteine. These results suggest that in *Neurospora* the biosynthesis of cysteine involves the coupling of sulfate to an organic compound followed by the reduction of the sulfur.

In each case crosses have shown that each mutant differs from wild type by a single gene, and that these genes are non-allelic.

POWERS, E. L., JR., and DEBORAH SHEFNER, Argonne National Laboratory, Chicago, Ill.: *Lethal changes induced by X-rays in Paramecium aurelia*.—Cultures of *P. aurelia*, stock 51, "killer" animals of variety 4, mating type VIII were irradiated with 250KV X-rays at about 450 r/minute at 17 dose levels from 500 to 25,000 r. Lines derived from isolates from each of the irradiated cultures were allowed to go into autogamy and the fractions of the

surviving exautogamous organisms were noted. Death following autogamy increases with increasing dose. Above 12,000 r the curve approaches 100 percent death very slowly, total death not being achieved in these experiments. Organisms which survived autogamy showed only control death following the next autogamy regardless of the degree of effect. Conjugation of irradiated with nonirradiated organisms resulted generally in increased survival following the next autogamy. These two results are expected if the effect of X-rays at these dose levels are genetic ones in the micronucleus. No significant difference can be seen between the genetic damage induced by X-rays as demonstrated here and that caused by beta particles of radioactive Strontium and Yttrium in solution as reported previously.

PREER, J. R., JR., University of Pennsylvania, Philadelphia, Pa.: *Microscopic bodies in the cytoplasm of "killers" of Paramecium aurelia and evidence for the identification of these bodies with the cytoplasmic factor, kappa*.—Killers possess the cytoplasmic factor kappa and liberate paramecin into the fluid in which they live. Sensitives lack kappa and are killed by paramecin. Feulgen positive bodies which probably represent kappa have been found in killers. After acid hydrolysis or ribonuclease digestion the bodies stain well with Giemsa stain. That the bodies contain desoxyribonucleic acid is shown by the positive Feulgen reaction and by the fact that they do not stain with Giemsa if digested with ribonuclease and then desoxyribonuclease. Specificity of the desoxyribonuclease is indicated since the stainability of the bodies is removed by the enzyme preparation only if magnesium is present. Strong killers of one stock contain approximately 1000 bodies per animal. The bodies differ in different killer stocks, but in general, appear as minute, spherical to ovoid particles, often double. Single forms vary from 0.2–0.8 micron. In some killer stocks their structure and size is fairly uniform; in others they are very variable—but most of the killer stocks have characteristic types of bodies. The appearance of the double forms suggests that the bodies reproduce by doubling. The bodies are invariably and quantitatively associated with the killer character and kappa; they are never found in animals lacking kappa. Experimental variation of kappa concentration by differential multiplication rate and by X-radiation reveals a parallel variation in concentration of the bodies. In number, size, probable chemical constitution, and probable self-reproductive nature, kappa and the bodies are identical. Therefore it is highly probable that the bodies represent kappa.

ROBINSON, H. F., R. E. COMSTOCK, and P. H. HARVEY, North Carolina State College, Raleigh, N. C.: *The characterization of genotypic variances in corn*.—The experimental technic and results are presented of a study designed to provide estimates of the genotypic variance for eight characters in corn. The genotypic variance was separated into additive genetic variance and variance due to dominance deviations. Heritability was used to denote the additive genetic fraction of the total variance, expressed in percent. Estimates

of the degree of dominance were determined from the variance due to dominance deviations, relative to the additive genetic variance.

The present F_2 plants and F_3 progeny plots from 709 biparental crosses in three segregating single-cross hybrids supplied the data for computing the various estimates. The characters investigated were plant height, ear height, husk extension, husk score, ear number, ear length, ear diameter and yield. Three estimates of heritability for each character were obtained by using (1) components of variance from the analyses of the F_3 progeny data, (2) covariance analysis of the F_2 female parent and F_3 progeny plot values, and (3) covariance analyses of the F_2 male parent and F_3 progeny plot values.

The estimates of heritability for plant and ear height and husk characters were all relatively high compared to similar values obtained for yield and ear characters.

Little or no dominance was indicated for genes affecting the development of plant and ear height. The genes concerned with the development of length and number of ears were estimated to have partial dominance whereas complete dominance was signified for genes involved in the expression of ear diameter, husk extension and husk score. Over-dominance was indicated for genes affecting yield; however, the magnitude of the standard error associated with this value would not preclude the possibility of obtaining such a result from genes having no more than complete dominance.

ROGERS, C., University of Delaware, Newark, Del.: *The effects of the mutant small-wing on cell size and diploid male mortality in Habrobracon*.—Studies of diploid males, homozygous and heterozygous for the mutant small-wing give opportunity to test the validity of the hypothesis that diploid male mortality is strictly related to cell size. The mutant small-wing is characterized by shorter wings and smaller wing cells. Counts show that the homozygous small-wing diploid males, with smaller cells, and the heterozygous diploid males, with larger cells, are equal in viability. It is suggested, therefore, that explanation of diploid male mortality, strictly in terms of cell size and the nucleocytoplasmic ratio is inadequate.

RUBIN, BENJAMIN A., Brookhaven National Laboratory, Upton, Long Island, New York: *Detection of the mutagenic effect of transmutation*.—Recent work of POWERS, ZIRKLE, STAPLETON and others indicates that certain absorbed radioactive elements produce greater biological effect than can be expected from ionization alone. This effect has been attributed to the increased specific ionization arising from the selective absorption of biologically important elements.

An alternative explanation is necessary if it can be shown that the increase of ionization due to selective absorption is insufficient to account for the addition effect. This alternative is sought by calculating the total ionization occurring within a sensitive volume. In a small object within a much larger volume of a radioactive solution, the specific ionization may be viewed as the sum of the effects arising from the suspending medium plus the ionization

resulting from disintegrations within the small body. The specific ionization in the large volume is corrected by subtracting surface losses determined for an infinite plane. In the small body whose greatest dimension is much less than the average beta track, it has been possible to calculate the specific ionization from disintegrations arising from within. From the quantitative assay of the beta-emitter after biological concentration has occurred, the ionizing effect of this increment is computed. The presence of an effect much beyond that expected from the total calculated ionization may now be attributed to another force—in this case probably transmutation.

Sample calculations and experimental data are presented.

RUSSELL, ELIZABETH S., ELIZABETH L. FONDAL, and JANE L. COULOMBRE, Jackson Memorial Laboratory, Bar Harbor, Maine: *Preliminary analysis of pleiotropism at the W-Locus in the mouse.*—Substitutions among alleles at the W-locus (W , W^v , w) are responsible for gross changes in several apparently independent characters: number and size of red-blood corpuscles; duration of life; fertility; and intensity and extent of pigmentation. The variations of each character can be studied quantitatively, eventually on an isogenic background. This present pilot experiment on non-inbred material reports the red-cell number characteristic of each genotype, the histology of the developing gonad in each, and the nature of the effect of each genic substitution on pigmentation. From these data and pertinent facts in the literature, suggestions are made of possibilities for sites of original W gene action and of ways of testing among these and of following the course of the developing pleiotropism by experimental methods.

RUSSELL, LIANE BRAUCH, and W. L. RUSSELL, Oak Ridge National Laboratory, Oak Ridge, Tenn.: *The production of phenocopies in the mouse by means of X-ray treatment of embryos.*—Mouse embryos in various stages of development were treated by subjecting pregnant females to 250 kvp X-rays (total body irradiation). The females used were 2–17 days gravid as timed from the observation of vaginal plugs. Using total doses of 200–500 r and intensities mostly between 72–84 r/minute, characteristic and consistent results were obtained for various stages of embryonic life treated. Raying on the 9th, 10th, 11th and 12th days, the stages most investigated at the present time, produces abnormalities which resemble, in many of their features, the effects of known gene mutations. These induced abnormalities, some of which are similar to ones described by KAVEN, are being studied in greater detail. Among those which, as far as we know, have not been recorded before is a syndrome characterized by oligodactylism and resembling the description of a mutant reported by HERTWIG.

RUSSELL, W. L., Oak Ridge National Laboratory, Oak Ridge, Tennessee and Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine: *Maternal influence on number of lumbar vertebrae in mice raised from transplanted ovaries.*—Earlier studies on reciprocal hybrid differences in number of lumbar vertebrae could not distinguish between two possible causes: maternal environment

and cytoplasmic inheritance. The present experiments have shown the existence of a maternal effect. Ovaries from inbred 129 strain mice were transplanted to the ovarian capsules of $129 \times B \text{ alb } C F_1$ hybrids whose own ovaries were removed. The hosts were then mated to strain 129 males, thus producing 129 strain offspring raised in hybrid foster mothers. Control transplantations were made within the 129 strain to uncover any influence that might result from the ovaries or host females being affected by the operation itself. The forced heterozygosis of chinchilla and albinism maintained in the 129 strain provided all experiments with genetic markers that distinguished offspring of transplanted ovaries from offspring of regenerated host ovaries.

Comparing 2112 animals of the 129 strain with 577 offspring of control transplantations within the strain, there is no significant difference in average number of lumbar vertebrae, indicating no effect of the operation itself. Comparison of these two groups with 1544 skeletons of 129 strain animals raised in $129 \times B \text{ alb } C$ hybrid hosts shows a significantly lower average in the hybrid-raised offspring, the effect being consistent throughout both sexes and all of three subgroups of the 129 strain. Another experiment, yielding 611 skeletons of 129 strain raised in $129 \times C57$ black hybrids, gave similar results. It is concluded that the skeletal effect observed in each experiment is caused by a difference in the maternal environments.

SHOWALTER, A. M., Madison College, Harrisonburg, Va.: *Inheritance of fruit shape in a variety of Cucurbita mochata*.—Two widely divergent types as to fruit shape were derived by selection and inbreeding from a pear shaped type. One type has long thick neck and small seed cavity. The other has no neck and large seed cavity. When these are crossed the F_1 fruits are of intermediate shape. Probably several genes without dominance are indicated.

SMITH, BEN W., North Carolina State College, Raleigh, N. C.: *Hybridity and apoimixis in the perennial grass, Paspalum dilatatum*.—Morphological uniformity marks the "common" cultivated variety of *Paspalum dilatatum* Poir. Ascending culms, ciliated spikelets, purple anthers and ergot susceptibility characterize the species as it occurs in North America, Australia, and South Africa. Identical characters exist in most material collected from its native Rio La Plata-Parana region. Two other varieties occur in Uruguay: (1) an erect yellow-anthered type and (2) a semi-prostrate, sparsely ciliate type with short internodes.

The common type appears equally uniform in its consistently irregular meiosis. With $2n=40$ in a genus with $x=10$, there are typically 30 elements, $10_{II} + 10_1 + 10_1$ at diakinesis and metaphase I. The bivalents disjoin normally; ten of the univalents divide mitotically at metaphase. The ten remaining univalents divide later; eight to ten of these lag in the equatorial region and eventually disintegrate during telophase and interkinesis. The homeotypic division and tetrad formation are essentially normal; very few micronuclei occur.

The semi-prostrate variety, *pauciciliatum* Parodi, resembles "common" at metaphase I, but approximately 20 chromosomes lag while the bivalents disjoin and proceed to the poles. The yellow-anthered type has a normal meiosis

with 20 pairs at metaphase I. The three morphologically distinct types are equally distinct cytologically.

The widely distributed "common" population, presumably hybrid in origin, is maintained by agamospermy; apospory is followed by diploid parthenogenesis. Multiple embryo sacs occur. One to six percent twin and triplet seedlings are found; these appear identical. The role of pollination is problematical; seed develop in isolated, emasculated florets.

Polyploidy, meiotic irregularity, and probably apomixis are frequent in the predominately tropical genus *Paspalum*.

SMITH, LUTHER, R. S. CALDECOTT, and BARBARA HAYDEN, State College of Washington, Pullman, Washington: *Experimental modification of the biological effects of X-rays*.—Tests with dormant and germinating seeds of barley and einkorn have shown that the atmosphere surrounding seeds during X-raying, or heat either before or after X-raying, profoundly modifies the effects of the irradiation. Three criteria were used in making the comparisons: 1) Injury symptoms, 2) Frequency of chromatinic bridges in root-tip cells, 3) Frequency of seedling mutants in F_2 . Seeds irradiated in a vacuum or atmosphere of nitrogen were affected less than seeds given the same treatment in the presence of air. A most unexpected result was obtained when seeds which were given a lethal heat treatment were "resuscitated" by subsequent X-radiation. It was also found that X-raying seeds before they were given a lethal heat treatment "protected" them from inactivation by heat at some X-ray dosages. The "protection" was strongly dependent on dosage and seemed to follow a cyclic pattern. It was also found that a heat treatment that was only a little short of killing seeds reduced by 50 percent the frequency of chromatinic bridges in cells of root tips grown from X-rayed seeds. This reduction in bridge frequency was obtained by heat treatments applied either immediately before or after the X-radiation. A heat treatment applied after X-radiation increased the seedling mutation rate from 5.8 ± 0.6 to 9.1 ± 0.6 percent. The same heat treatments applied before the irradiation increased the mutation rate only to 6.9 ± 0.6 percent. Thus, the treatment (X-radiation only) that gave the highest frequency of bridges in root-tip cells gave the lowest frequency of mutations.

STALKER, H. D., and H. L. CARSON, Washington University, St. Louis, Missouri: *Seasonal changes in gene arrangement frequencies and morphology of *Drosophila robusta**.—Salivary gland chromosome studies of F_1 larvae of wild flies from Olivette, St. Louis County, Missouri showed that three of the fourteen gene arrangements found in chromosomes X, 2 and 3 showed significant frequency changes during 1946. Two of these (2L-2, SL-3) assumed new frequencies maintained since 1946; in the third (3R vs. 3R-1) the frequency of 3R-1 rose in the fall of 1946 but returned to its original level in the spring of 1947.

Morphological studies of 500 F_2 progenies of wild females showed: (1) A significant, regular morphological change during 1946 from May through August; F_2 individuals from females captured in the early summer showed morphological resemblance to northern races. Since F_2 individuals were

reared under standard laboratory conditions, the change apparently has a genetic basis, and may have been produced by natural selection of the southern type during the summer. (2) Correlations between gene arrangements and morphology were found in two (2L vs. 2L-1 and XR vs. XR-1) of four cases tested. Since frequencies of these arrangements did not change during 1946, whereas the morphology did, it is unlikely that all the genes controlling the observed morphological changes are located within them. (3) None of these four arrangements was associated with "northern" vs. "southern" phenotypes, although all four show north-south frequency clines. Thus, at present there is no evidence that the previously observed geographical gradient in morphology is based on the inversion frequency gradient.

STEINITZ, LOTTI M., University of Wisconsin, Madison, Wisconsin: *A comparative study of chromosomes of Hemizonia virgata, Gray, under greenhouse conditions and in sterile culture.*—Chromosome morphology and differentiation of root nuclei and tissues of a clone of *Hemizonia virgata* is the same in excised roots growing at different rates under sterile conditions in two simple nutrient media which differ only by the addition of 0.1 percent casein hydrolysate. The demonstration compares these with those of roots of *Hemizonia* plants growing under greenhouse conditions.

STEPHENS, S. G., Texas Agricultural Experiment Station, College Station, Texas: *A new interpretation of panicle morphology based on a study of a dwarf mutant in corn.*—A dwarf mutant gene in corn, in addition to reducing internode length, delays the production of lateral ear shoots, so that the "sterile zone" normally existing between top-most ear shoot and lowest lateral branch of the tassel tends to be eliminated. Consequently, *in the mutant*, an almost continuous series of axillary branches extends from base to apex of the main stem. A comparative morphological study of this series shows that ear and tassel structure results from a combination of a progressive reduction of axillary branches and a progressive condensation of nodes, both these tendencies being initiated during the vegetative phase. It is suggested that the same processes occur more rapidly, and are synchronized more closely with the switch from vegetative to reproductive phase *in the normal plant*.

STEPHENS, S. G., Texas Agricultural Experiment Station, College Station, Texas: *Gene divergence in the control of flower pigmentation in cotton.*—Neighboring loci concerned with anthocyanin pigmentation of the cotton flower control similar chemical processes but act on slightly different substrates. This suggests they originated as repeats accompanied by divergence in function—Genetics 33: 191-214 (1948). Arch. Biochem. (in press). A study of a second, genetically independent system controlling anthoxanthin pigmentation can be interpreted similarly, although cytological support is still lacking. A pseudo-allelic basis is probable, however, as two genes apparently control the production of isomeric pigments, and, in combination, produce a third pigment which structurally may be regarded as an internally compensated "hybrid" of the two isomers. The "hybrid" pigment is also produced independently by a

third, dominant, member of the pseudo-allelic series. Divergence in function of loci has apparently accompanied speciation.

STORMONT, CLYDE, University of Wisconsin, Madison, Wisconsin: *The J substance, an acquired character of cattle erythrocytes.*—Among the numerous, gene-controlled, serological characters of cattle erythrocytes, that called J is unique in the following ways. (1) It has been detected only by reaction with normal antibodies. All others are recognized by immune antibodies. (2) It has been found not only in erythrocytes but in soluble form in the plasma of J-positive individuals. (3) It has not as yet been detected in the cells of newborn calves. (4) Quantitatively, it varies markedly among adults but appears to be constant within individuals. (5) Twins having a mixture of each other's blood (presumably due to an exchange, during fetal life, of those cells which produce erythrocytes), and therefore presumably having identical blood-types, may differ in that the two kinds of erythrocytes of one twin may lack the J factor while the cells of the co-twin may possess J. Apparently, if the gene for the J substance is present in one twin and not in the other, both kinds of erythrocytes will carry the character in the twin with the gene, while in the co-twin which lacks the gene for J neither of the two kinds of erythrocytes possesses J. The gene seemingly produces its effect in tissues other than the blood, and the cells presumably acquire the J character in contact with the plasma. In this respect, it has been possible to demonstrate that erythrocytes lacking J may acquire it from plasma either *in vivo* or *in vitro*. Similarity in reactivity has been noted between the J substance of cattle and the A of humans.

TAYLOR, J. HERBERT, University of Tennessee, Knoxville, Tenn: *Chromosome behavior and structure as revealed by meiosis in cultures of excised anthers.*—Excised anthers from a clone of *Tradescantia paludosa* were grown in tissue culture. Many of the anthers excised during early stages of meiosis progress through both divisions and occasionally form microspores. Meiotic divisions in cultures at 25°C and 30°C are essentially normal as compared to those occurring in buds from plants grown in the greenhouse. However, anthers excised during zygotene and pachytene often show a marked increase in inlocking bivalents at diakinesis. There is also greater variation in chiasmata frequency at diakinesis, occasionally both increases and decreases being found in the same anther. These cultured anthers often show spiral structure with unusual clarity and prophase stages are seen in better detail than in normal *Tradescantia*, which is characteristically almost impossible of analysis. Anthers excised at leptotene may produce a high percentage of univalents at diakinesis. In all cases of continuing differentiation thus far examined, anthers excised while the sporogenous tissue is still actively mitotic and grown at 30°C pass through a modified meiosis in which there are only univalents at diakinesis. The synchronization of microsporocyte divisions typical of *Tradescantia* is lost and stages similar to normal meiosis are seen varying from leptotene to diakinesis in one anther. Since typical zygotene and pachytene are absent, it appears that synapsis fails, while the spiralization cycle and physiological state of these cells is similar to normal microsporocytes.

TEAS, H. J., Oak Ridge National Laboratories, Oak Ridge, Tennessee: *The genetics of threonine requiring mutants of Neurospora crassa.*—Three *Neurospora* mutants shown to differ from wild type by a single gene have growth requirements as follows: strain 51504 uses threonine plus methionine or homoserine alone; strain 44104 uses alpha-aminobutyric acid, isoleucine, or threonine; and strain 35423 uses only threonine. Mutant 51504 shows linkage with the first or sex chromosome, giving no recombinations with aurescent in 67 asci; mutants 44014 and 35423 show no linkage with the first or fourth chromosomes, but the genes involved in these mutants are apparently linked with each other. The latter two mutants gave centromere distances of 25 and 2 units respectively when outcrossed to one strain (12a) and 0 and 13 units respectively when outcrossed to another strain (34508, aurescent). Samples of asci were checked for bad spore types and an analysis was made of all the asci dissected. It was found that the failure to detect a crossover in 34 asci from the cross of 44104 with 35423 as well as the differences in centromere distance could not be explained on the basis of selection of asci for genetic analysis. It is suggested that mutants 44104 and 35423 differ in that one of them carries a suppressor of crossing over which is ineffective when homozygous.

VICARI, E. M., Jackson Genetic Laboratory, Bar Harbor, Me.: *Age threshold of gene controlled sonogenic convulsion in mice modified by endocrine action and associated with physiologic threshold.*—Previous studies by the writer demonstrated that age was a vital factor in the susceptibility to fatal sonogenic convulsions in mice. That, moreover, the age susceptibility was at different levels for different genetic strains of mice. This report deals with an attempt made to defer, prolong or retard the age threshold by shifting the physiologic threshold. The experimental approach was through endocrine action.

From the experimental data the following results may be drawn: (1) pre-convulsive period was lengthened, (2) activity pattern was altered, (3) emotional pattern was modified, (4) a recovery period and paralytic effects were substituted for fatal seizure, (5) percent fatality was reduced around 40 percent in the males and 90 percent in the females, (6) no apparent relation existed between susceptibility to convulsive reactions and susceptibility to cancer, (7) there were indications of some steroid function in the convulsive pattern.

VILLEE, C. A., and M. D. LOWENS, Harvard Medical School, Boston, Mass.: *Barbituric acid as an inhibitor of growth and pupation in Drosophila.*—Previous experiments (VILLEE and BISSELL, *Jour. Biol. Chem.*, **172**: 59, 1948) have shown that benzimidazole, chemically similar to the purines, when added in place of ribonucleic acid (RNA) to the chemically defined medium for the growth of *Drosophila*, delayed the pupation and hatching of the larva or caused its death. In another series of experiments using the same technique and substituting barbituric acid, chemically similar to the pyrimidines, for RNA in the medium described previously, it was found that this substance, when present in concentrations of 1 mg/ml or 0.1 mg/ml delayed pupation of wild type flies to 20 to 50 percent longer than flies grown on the control medium

with RNA. As with benzimidazole, vestigial flies were inhibited to a lesser degree than were wild flies. Barbituric acid in a concentration of 1 mg/ml produced a 20 percent increase in the egg-pupa time of vestigial flies. This delay was partially overcome by the addition of RNA 1 mg/ml but not by the addition of adenine 1 mg/ml. Since the previous experiments had shown that adenine is an almost complete substitute for RNA, the fact that RNA but not adenine overcame the growth inhibition of barbituric acid suggests that the latter inhibits because it is a structural analogue of the pyrimidines and that the inhibition is reduced by the pyrimidines present in the RNA.

WALLBRUNN, HENRY M., University of Chicago, Chicago, Ill.: *Genetics of Betta splendens* I.—The color of the Siamese fighting fish is due to pigments in melanophores, erythrophores, and xanthophores, and to light refracted by crystals in guanophores. In my stock I have found no xanthophores. Three colors of guanophores corresponding to the two homozygous and heterozygous cases occur. I have named the locus *G*; *GG* giving steel-blue; *gg*, green; and the heterozygote, *Gg*, blue. The *G* locus determines the color produced by guanophores, but their distribution is determined by at least two other loci. Locus *a*, and locus *s* determine the extent of guanophore distribution on the fins and body, respectively. The *aa* fish have solid blue, steel-blue, or green fins because of the great density of guanophores which overlie the ever-present erythrophores and often-present melanophores. *AA* fish have large, pure red fin areas with guanophores in restricted but definite areas. *Aa* fish are either identical with or very similar to *AA*. Exact determination has been impossible up to the present, because of complications due to the *S* gene which has a slight effect on the fin guanophores as well as on the body. The *s* locus proved to be more easily worked out in fish with no melanophores which are homozygous *c*; *ss cc* fish have a sparse body covering of guanophores. *SS cc* have a much denser covering of guanophores and also an uneven clumping of them so that some scales and spots in the fins are darker than surrounding areas. *Ss cc* fish have a more even color distribution but approach *SS* more closely than *ss*.

WATSON, J. D., Indiana University, Bloomington, Indiana: *Inactivating mutations produced by X-rays in bacteriophages*.—LURIA reported in 1947 that reactivation by multiple infection, such as he discovered for ultraviolet inactivated bacteriophages, could not be detected after X-ray inactivation. In reinvestigating this problem, we found that X-rays, besides inactivating phage, also suppress the ability of phage to infect bacteria, one "adsorption suppressing" hit occurring on the average for every three inactivating hits. Because of this, reactivation is difficult to detect by the multiple-infection technique. We tested for it by infecting individual bacteria with one particle *T2r⁺* inactivated by X-rays and one particle *T2r* inactivated by ultraviolet. A significant proportion of these bacteria liberate a mixture of active *T2r⁺* and active *T2r*, which proves that X-rayed phage can participate in genetic recombination and reactivation. Similar conclusion was reached by infecting bacteria with one active particle *T2r⁺* and one X-rayed particle *T2r*. Finally, reactivation was also detected by mixed infection with one particle each of X-ray inactivated

T2r⁺ and *T2r*. Quantitatively, we found that for equal numbers of inactivating hits, the contribution of an X-ray inactivated particle to reactivation is lower than that of an ultraviolet inactivated one. The relative contribution of X-ray and ultraviolet inactivated particles is constant in all types of experiments listed above. This result might be an indication that one X-ray hit produces on the average more lethal mutations than one ultraviolet hit. If so, this would give experimental evidence for an actual difference in the spatial domain within which the genetic effects of one hit of each type can be exerted.

WHITING, P. W., University of Pennsylvania, Philadelphia, Pa.: *Simultaneous (?) mutations in an inbred stock of Habrobracon*.—In December 1944 three changes were noted in a closely inbred stock (sex alleles *xa/xb*) which had been under observation for over three years and in which wild type and orange eye color and the female-sterile traits glass and sex-linked fused were being maintained. (1) A minus modifier appeared changing fused to semifused, midway between wild type and fused in the male, weakly fertile in the female. This modifier proves to be linked in the orange group. (2) There was a sudden drop in fecundity of the females. Records of 40 with normal life span showed nine sterile, 10 with less than 10 progeny each and only 7 with over 30. After further breeding normal fecundity was recovered. (3) There was a marked increase in ratio of diploid males to females—23:24 (95.8 percent relative viability) in one "large" fraternity. Twelve small fraternities totalled 42:63 (66.7 percent). As fecundity was recovered, the ratio of diploid males to females dropped, 40 fraternities showing 693:1735 (39.9 percent). Subsequent selection showed 15 with 239:412 (58.0 percent) and unselected material showed 41 with 219:674 (32.5 percent). Culture temperature tests with this material proved inconclusive. At 29°C 14 fraternities showed 90:235 (38.3 percent relative viability); at 22°C 15 showed 84:201 (41.8 percent); at 32°C 14 showed 276:780 (35.4 percent). Counts within the stock previous to the mutation had shown only 19:1292 (1.5 percent).

WHITTINGHILL, MAURICE, Department of Zoology, University of North Carolina, Chapel Hill, N. C.: *The effects of methyl-bis (b-chloroethyl)amine upon recombination values in Drosophila melanogaster*.—Adult *D. melanogaster* females of the constitution *ru h th st cu sr e⁺ ca*/wild were subjected to a sublethal dose of an aerosol of methyl-bis(b-chloroethyl)amine in cyclohexane and were then testcrossed in five successive sets of four-day cultures. The majority of the treated females were sterile. Recombinations in the spindle attachment region, *st-cu*, rose to 33 ± 3.7 per cent, about 5×normal value, and remained at that level through all subsequent cultures. In all regions between *h* and *e⁺*, treated families had more crossover than controls had, although increases outside the spindle region were slight. The distal regions, however, both showed a decrease in recombination in the treated families. The proximal increases and distal decreases were well represented in the offspring from eggs laid only four to eight days after exposure. This nitrogen mustard seems to act sooner and more extremely than X-rays or other known effective agents.

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CORRIGENDA

Volume 32, 1947

Page 609, first column of table, insert "wild" before No. 51. . . .

Volume 33, 1948

Page 91, five lines from bottom, for "0.1r/min. against 0.017r/min." read "0.01r/min. against 0.0017r/min."

Page 227, nine lines from top, for "33657" read "33757."

Page 480, three lines from bottom, for "A" read "AA."

Page 481, seven lines from bottom, for "W" in denominator of formula read " \bar{W} ."

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- SWANSON, C. P. HOLLANDER, ALEXANDER, and KAUFMANN, B. N. Modification of the X-ray and ultraviolet induced mutation rate in *Aspergillus terreus* by pretreatment with near infrared radiation.

SEPTEMBER, 1948

- SHULL, GEORGE HARRISON, What is "Heterosis"?
- NEWCOMBE, HOWARD B., Delayed phenotypic expression of spontaneous mutations in *Escherichia coli*.
- CROW, JAMES F., Alternative hypotheses of hybrid vigor.
- LAUGHNAN, J. R., The action of allelic forms of the gene A in maize. I. Studies of variability, dosage and dominance relations. The divergent character of the series.

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